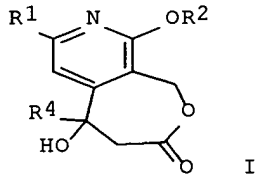
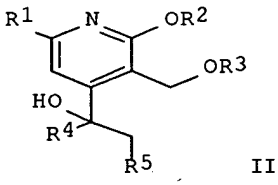
L4 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2003:173586 CAPLUS
DN 138:221736
TI Enantioselective synthesis of intermediates of (20R)-homocamptothecins and (20R)-homocamptothecins
IN Curran, Dennis P.; Gabarda, Ana E.
PA University of Pittsburgh, USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003018559	A2	20030306	WO 2002-US26424	20020819
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003073840	A1	20030417	US 2001-940059	20010827

PRAI US 2001-940059 A 20010827
OS CASREACT 138:221736; MARPAT 138:221736
GI



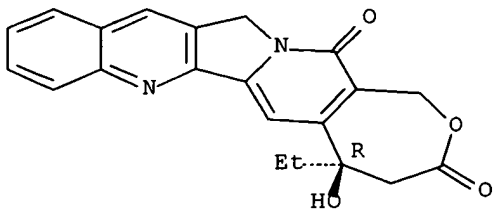
I



II

AB Intermediates of (20R)-homocamptothecins of formula I [R1 = H, F, Cl, trialkylsilyl; R2, R4 = alkyl] are prepd. from compds. of formula II [R3 = protecting group; R5 = carboxylic acid alkyl or aryl ester] by treatment with an org. acid or an inorg. acid.
IT **186669-19-2P**, (20R)-Homocamptothecin
RL: IMF (Industrial manufacture); PNU (Preparation, unclassified); PREP (Preparation)(enantioselective synthesis of intermediates of (20R)-homocamptothecins)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).


O
N
N
O
Et
R
HO
O

L4 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:927175 CAPLUS
DN 138:14131
TI Preparation of pharmaceutical compositions containing mikanolide, dihydromikanolide or an analog thereof combined with another anticancer agent for therapeutic use in cancer treatment
IN Prevost, Gregoire; Coulomb, Helene; Lavergne, Olivier; Lanco, Christophe; Teng, Beng-Poon
PA Societe De Conseils De Recherches Et D'applications Scientifiques (S.C.R.A.S.), Fr.
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002096348	A2	20021205	WO 2002-FR1800	20020529
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FR 2825278	A1	20021206	FR 2001-7104	20010530
PRAI FR 2001-7104	A	20010530		

OS MARPAT 138:14131
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

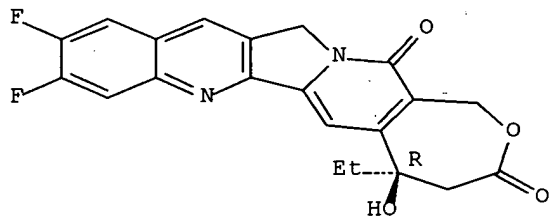
AB The invention concerns a product comprising at least mikanolide (I), dihydromikanolide or an analog, e.g., II [R1 = H, SR4, NR4R5; R2 = SR6, NR6R7; R3 = OH, O-acyl, O-silyl, O-carbamyl; R4, R6 = alkyl, cycloalkyl, (cycloalkyl)alkyl, hydroxyalkyl, (un)substituted aryl, aralkyl; R5, R7 = H, alkyl, cycloalkyl, (cycloalkyl)alkyl, hydroxyalkyl, (un)substituted aryl, aralkyl; R4R5 = 5- to 7-membered N-contg. ring] and III, or their pharmaceutically acceptable salts, combined with at least one other anticancer agent for simultaneous, sep. or prolonged therapeutic use in cancer treatment. In a preferred embodiment of the invention, the mikanolide, dihydromikanolide or one analog thereof is combined with enzymic inhibitors such as G heterotrimeric protein inhibitors, IV [X = R22; Y = R18; XY = 6-membered ring, CHR18CHR19; R11 = H, lower alkyl, alkylthio; R12, R13 = H, lower alkyl; R14 = O, H2; R5 = H, lower alkyl, (cycloalkyl)alkyl, alkenyl, alkynyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; R16, R17 = H, CONHCHR13CO2R14, lower alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; R18, R19 = H, lower alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl; R18R19 = aryl or heterocycly ring; R20, R21 = H, aryl, heterocyclyl, alkyl, arylalkyl, heterocyclylalkyl; R22 = NR9, S, O; R23 = ; R24 = H, lower alkyl], V

(R18,
R19 = H, lower alkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl;
R18R19 = aryl or heterocycly ring) or VI (R22 = NR9, S, O), or alkylating
agents such as cis-platin. Thus, VII was prepd. from mikanolide. VII was
tested for cell proliferation inhibition activity [only 34% of cells lived
when combined with VIII.cntdot.HCl (vs. human colon cancer HT-29 cells)].

IT **220997-97-7 220998-10-7**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antitumor agent; prepn. of compns. contg. mikanolide, dihydromikanolide or an analog combined with another anticancer agent for chemotherapy)

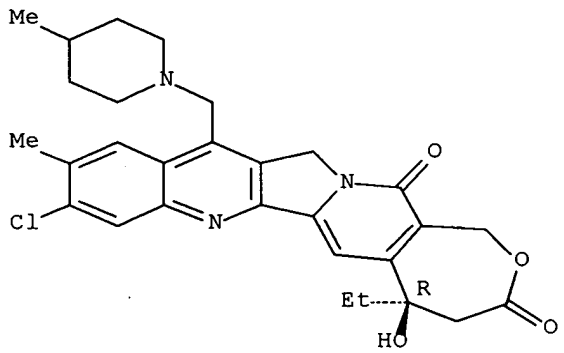
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 220998-10-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L4 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:814357 CAPLUS
DN 137:306988
TI Screening methods for identifying ligands
IN Stewart, Lancing J.
PA Emerald Biostructures, Inc., USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

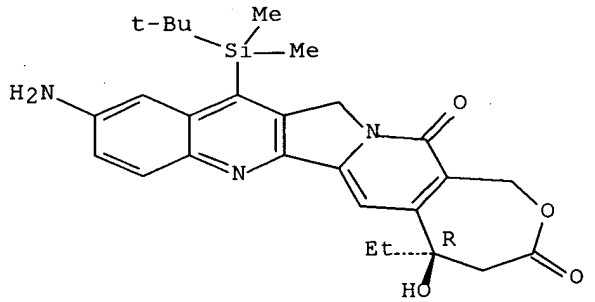
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002083938	A2	20021024	WO 2002-US11552	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002197628	A1	20021226	US 2002-121094	20020411
PRAI US 2001-283045P	P	20010411		

AB This invention relates to crystn. based assays for identifying ligands that bind to a macromol.

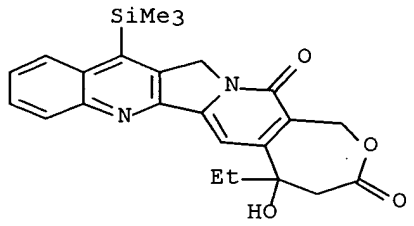
IT **428861-50-1**, AG260
RL: ARU (Analytical role, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); ANST (Analytical study); PROC (Process)
(screening methods for identifying ligands)

RN 428861-50-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

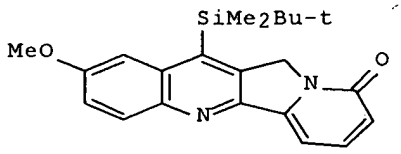
Absolute stereochemistry. Rotation (+).



L4 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:634098 CAPLUS
DN 138:255385
TI Development of new camptothecin analogs as cancer chemotherapeutic agents:library synthesis of homosilatecans and the first asymmetric synthesis of homocamptothecin and related homosilatecans
AU Gabarda Ortega, Ana Esther
CS Univ. of Pittsburgh, Pittsburgh, PA, USA
SO (2001) 202 pp. Avail.: UMI, Order No. DA3026025
From: Diss. Abstr. Int., B 2002, 62(9), 4021
DT Dissertation
LA English
AB Unavailable
IT **300582-87-0DP**, derivs. having a diverse range of functions at the C7 and C10 positions
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(homosilatecans, library synthesis; library synthesis of homosilatecans and the first asym. synthesis of homocamptothecin and related homosilatecans in the development of new camptothecin analogs as cancer chemotherapeutic agents)
RN 300582-87-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:624707 CAPLUS
DN 137:325546
TI Palladium-Promoted Cascade Reactions of Isonitriles and 6-Iodo-N-propargylpyridones: Synthesis of Mappicines, Camptothecins, and Homocamptothecins
AU Curran, Dennis P.; Du, Wu
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Organic Letters (2002), 4(19), 3215-3218
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English
OS CASREACT 137:325546
GI



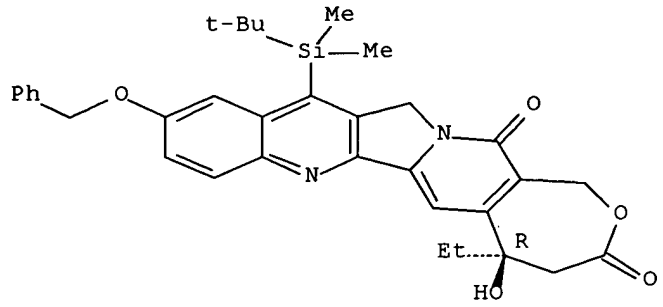
I

AB Ambient-temp. reactions of electron-rich aryl isonitriles with substituted 6-iodo-N-propargylpyridones in the presence of silver carbonate and palladium acetate produce 11H-indolizino[1,2-b]quinolin-9-ones, e.g. I, in good to excellent yield. Exptl. evidence suggests that the process occurs though organopalladium rather than radical intermediates. It is applied to synthesis analogs of mappicine and camptothecin, including the silatecans DB-67 and DB-91 (homo-DB-67).

IT **472961-12-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of mappicines, camptothecins, and homocamptothecins via palladium-promoted cascade reactions of isonitriles and 6-iodo-N-propargylpyridones)

RN 472961-12-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

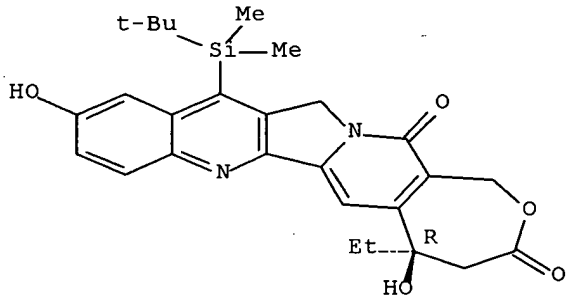


IT **247043-98-7P**, DB 91
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of mappicines, camptothecins, and homocamptothecins via palladium-promoted cascade reactions of isonitriles and 6-iodo-N-propargylpyridones)

RN 247043-98-7 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, (5R)- (9CI) (CA INDEX NAME)

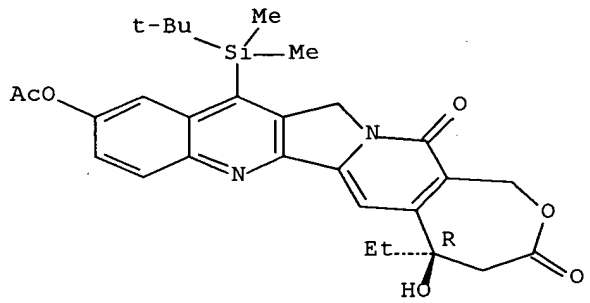
Absolute stereochemistry. Rotation (+).



RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

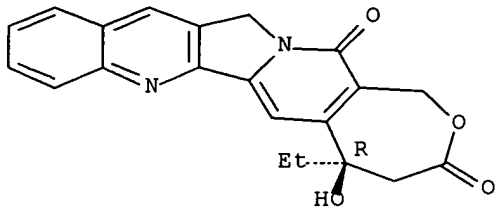
L4 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:585460 CAPLUS
DN 137:311068
TI Asymmetric total synthesis of (20R)-homocamptothecin, substituted homocamptothecins and homosilatecans
AU Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Tetrahedron (2002), 58(32), 6329-6341
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
AB An efficient asym. synthesis of a key DE lactone pyridone intermediate in the synthesis of homocamptothecin is reported. The synthesis is scalable and features a Stille coupling and a Sharpless asym. epoxidn. as the key steps. The key intermediate was parlayed into homocamptothecin and an assortment of fluorinated homocamptothecins and homosilatecans (7-silylhomocamptothecins), thereby providing the first asym. entry to this important new class of antitumor agents.
IT **472958-54-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. total synthesis of (20R)-homocamptothecin and analogs through a key DE lactone pyridone intermediate using a Stille coupling and a Sharpless asym. epoxidn.)
RN 472958-54-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



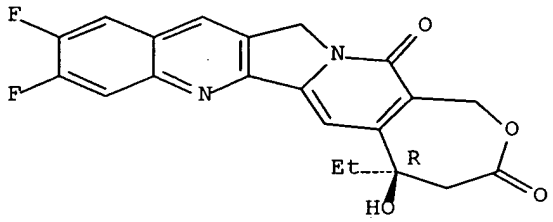
IT **186669-19-2P**, (20R)-Homocamptothecin **220997-97-7P** **247043-98-7P** **284684-27-1P** **284684-28-2P** **284684-29-3P** **284684-31-7P** **428861-50-1P** **472958-66-0P** **472958-67-1P** **472958-68-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. total synthesis of (20R)-homocamptothecin and analogs through a key DE lactone pyridone intermediate using a Stille coupling and a Sharpless asym. epoxidn.)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



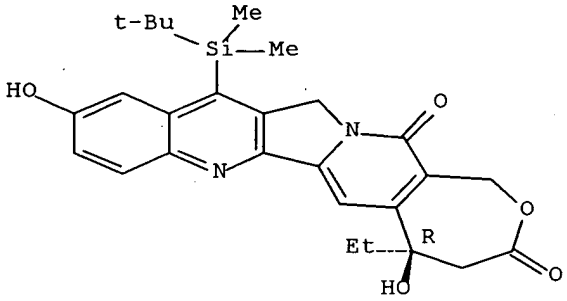
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



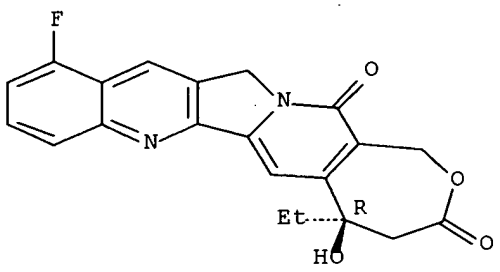
RN 247043-98-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



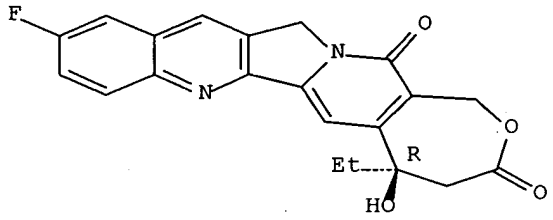
RN 284684-27-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-11-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



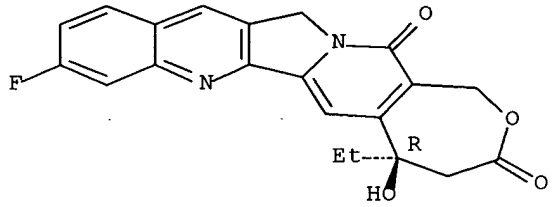
RN 284684-28-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



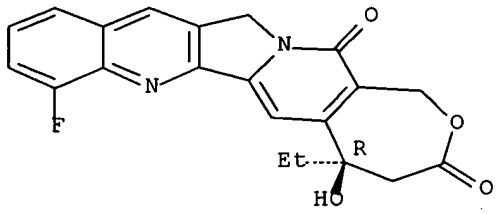
RN 284684-29-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



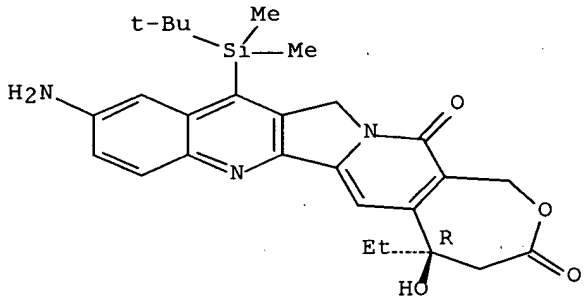
RN 284684-31-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-8-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



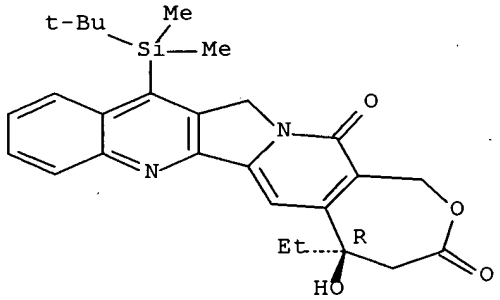
RN 428861-50-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



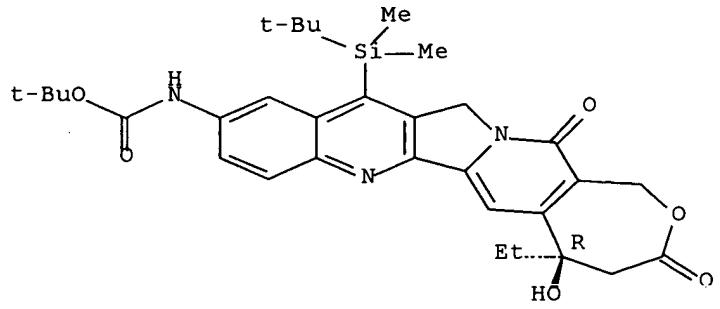
RN 472958-66-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 472958-67-1 CAPLUS
CN Carbamic acid, [(5R)-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

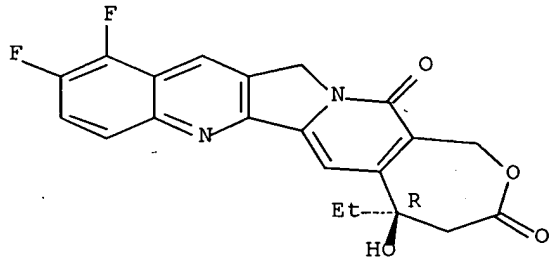
Absolute stereochemistry. Rotation (+).



RN 472958-68-2 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

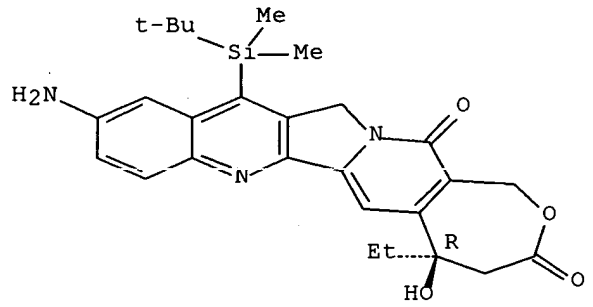
L4 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:391861 CAPLUS
DN 136:397871
TI Crystal structure of topoisomerase I complexes with DNA and inhibitors and
use in designing new anti-cancer agents and anti-microbial agents
IN Burgin, Alex; Hjerrild, Kathryn; Kim, Hidong; Staker, Bart Lee; Stewart, Lance; Behnke, Craig; Feese, Michael
PA Emerald Biostructures, Inc., USA
SO PCT Int. Appl., 468 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002040653	A2	20020523	WO 2001-US43550	20011114
	WO 2002040653	A3	20030130		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002019815	A5	20020527	AU 2002-19815	20011114
PRAI	US 2000-248474P	P	20001114		
	WO 2001-US43550	W	20011114		

AB This invention relates to cryst. structures of the topoisomerase I and their use in designing new anti-cancer agents and anti-microbial agents. It an object of this invention to solve the three-dimensional crystal structure of topoisomerase I in covalent complex with DNA and inhibitor compds. The invention relates to methods for identifying and designing topoisomerase I inhibitors which involves forming a crystal structure from the test agent and topoisomerase I covalently linked to duplex DNA at the topoisomerase I cleavage site and detg. the crystal structure of the complex to det. the spacial relationship of the topoisomerase I/DNA construct and the anti-cancer drug. The invention includes methods for designing topoisomerase I inhibitors which involves utilizing the crystal structure described above to design modified compds.
IT **428861-50-1D**, AG 260, complexes with topoisomerase I covalently linked to duplex DNA
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(crystal structure of topoisomerase I complexes with DNA and inhibitors and use in designing new anti-cancer agents and anti-microbial agents)
RN 428861-50-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-

tetrahydro-
5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



App'S

L4 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2002:39603 CAPLUS
DN 136:85980
TI Preparation of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents
IN Bigg, Dennis; Lavergne, Olivier; Pla Rodas, Francesc; Pommier, Jacques; Ulibarri, Gerard; Harnett, Jerry; Rolland, Alain; Liberatore, Anne-Marie; Lanco, Christophe; Cazaux, Jean-Bernard; Le Breton, Christine; Manginot, Eric
PA Societe De Conseils De Recherches Et D'applications Scientifiques (S.C.R.A.S.), Fr.
SO U.S., 53 pp., Cont.-in-part of U.S. Ser. No. 973,561.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 6339091	B1	20020115	US 1999-332520	19990614
WO 9700876	A1	19970109	WO 1996-FR980	19960621
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
ZA 9605318	A	19970124	ZA 1996-5318	19960621
EP 1251125	A2	20021023	EP 2002-77736	19960621
EP 1251125	A3	20021211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
FR 2757514	A1	19980626	FR 1996-15774	19961220
FR 2757514	B1	19990212		
FR 2757515	A1	19980626	FR 1996-15775	19961220
FR 2757515	B1	20000505		
FR 2768431	A1	19990319	FR 1997-10785	19970829
FR 2768431	B1	20000324		
US 5981542	A	19991109	US 1997-973561	19971202
WO 9828304	A1	19980702	WO 1997-FR2217	19971205
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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
WO 9828305	A1	19980702	WO 1997-FR2218	19971205
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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

	CN 1241192	A	20000112	CN 1997-180816	19971205
	CN 1090634	B	20020911		
	ZA 9711270	A	19980623	ZA 1997-11270	19971215
	WO 9911646	A1	19990311	WO 1998-FR1768	19980807
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	US 2002160994	A1	20021031	US 2002-61049	20020130
	US 2003004150	A1	20030102	US 2002-71046	20020206
PRAI	GB 1995-12670	A	19950621		
	WO 1996-FR980	W	19960621		
	FR 1996-15774	A	19961220		
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	FR 1996-15945	A	19961224		
	FR 1997-10785	A	19970829		
	US 1997-973561	A2	19971202		
	WO 1997-FR2217	W	19971205		
	WO 1997-FR2218	W	19971205		
	WO 1998-FR1768	W	19980807		
	US 1996-610476	A	19960304		
	EP 1996-924010	A3	19960621		
	FR 1999-2398	A	19990226		
	US 1999-332520	A3	19990614		
	WO 2000-FR461	W	20000224		
	US 2000-612382	A3	20000707		
	US 2001-806952	W	20010405		
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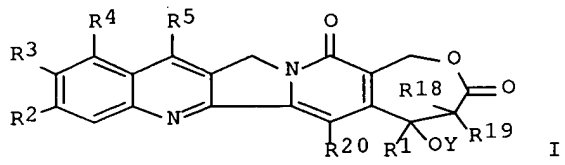
GI



I

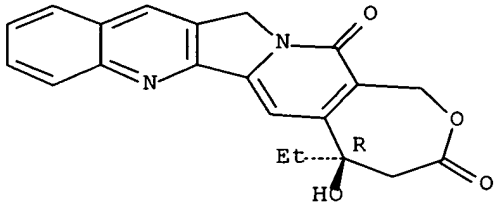
AB Camptothecin analogs, such as I [R1 = alkyl, alkenyl, alkynyl, haloalkyl, etc.; R2 = R3 = R4 = R5 = H, CN, NO2, NHNH2, N3, halo, cyanoalkyl, nitroalkyl, etc.; R18 = R19 = H, OH, halo, alkyl, alkoxy, etc.; R20 = H, halo; R21 = H, acyl; Y = H, CO-A-NR22R23; A = (un)substituted alkylene; R22 = R23 = H, alkyl, hydroxyalkyl, aminoalkyl, cycloalkyl etc.], and its non-toxic pharmaceutically acceptable salts, were prepd. and formulated as prodrugs for use as antitumor, antiviral, and parasiticidal agents. Thus, camptothecin analog I [R1 = Et; R2 = R3 = R4 = R5 = R18 = R19 = R20 = Y =

H (II)] was prepd. via a multistep synthetic sequence starting from (S)-(+)-camptothecin. The prepd. compds. were tested for topoisomerase inhibitory activity, (e.g. II shows 87.22 % inhibition of proliferation of tumor cell line L1210 at a concn. of 0.1 nM).

IT **186669-19-2P 186669-20-5P**
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents)

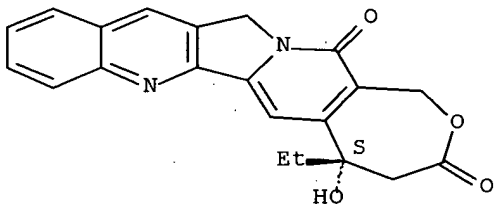
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



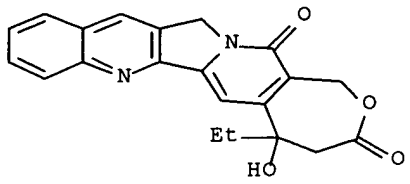
RN 186669-20-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

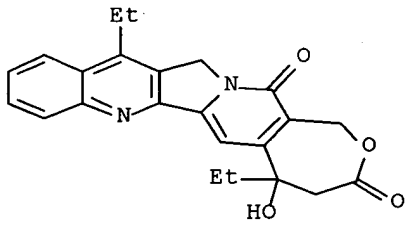


IT **186668-40-6P 186668-44-0P 186668-63-3P**
209909-08-0P 209909-09-1P 210563-32-9P
210563-43-2P 210563-57-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents)

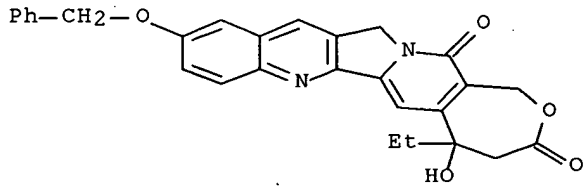
RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



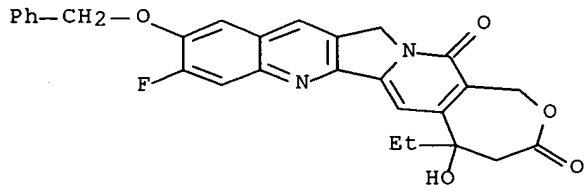
RN 186668-44-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-63-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)

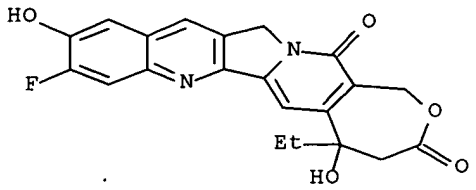


RN 209909-08-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)

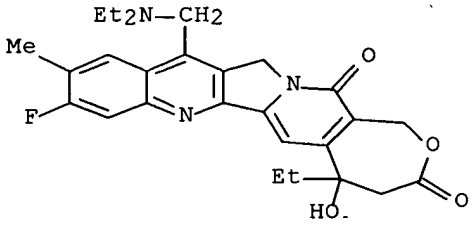


RN 209909-09-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX

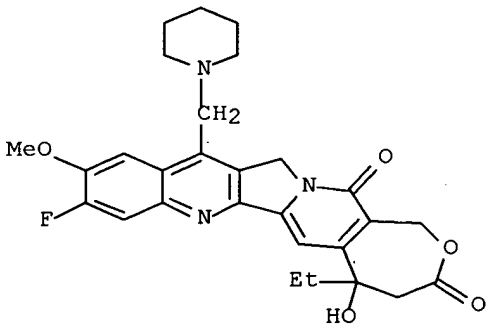
NAME)



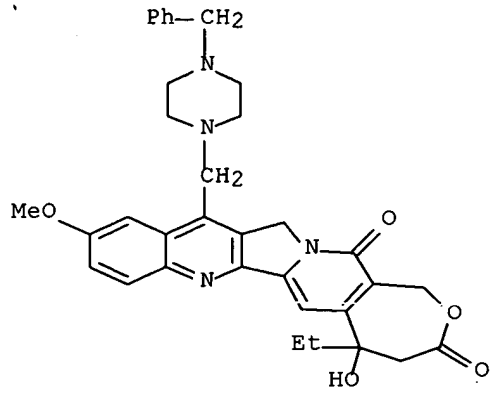
RN 210563-32-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(diethylamino)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



RN 210563-43-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



RN 210563-57-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



IT **186668-59-7P 186668-65-5P 186668-68-8P**
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186668-75-7P 186668-77-9P 186668-79-1P
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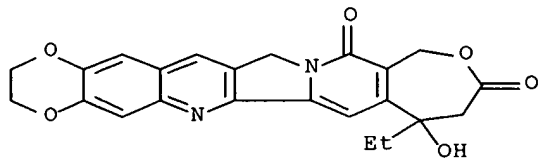
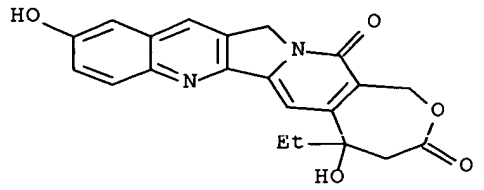
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents)

RN 186668-59-7 CAPLUS

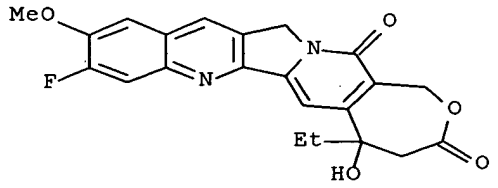
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)



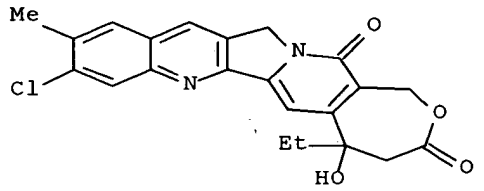
RN 186668-65-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



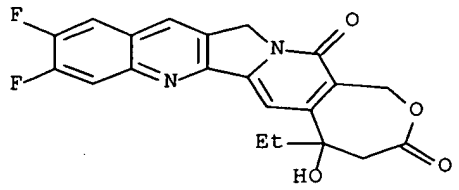
RN 186668-68-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



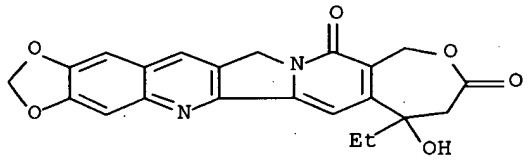
RN 186668-69-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



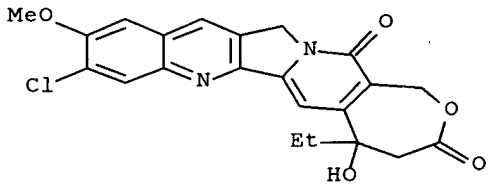
RN 186668-70-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



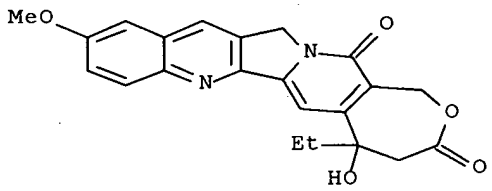
RN 186668-71-3 CAPLUS
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-
dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)



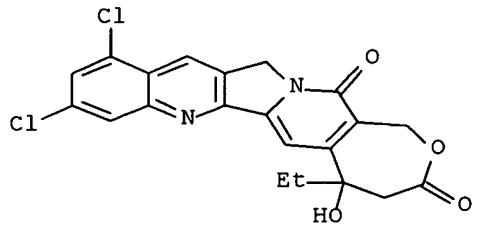
RN 186668-72-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



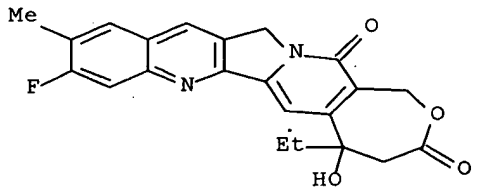
RN 186668-73-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



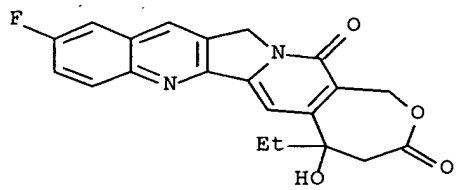
RN 186668-74-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9,11-dichloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



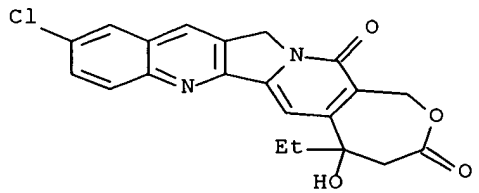
RN 186668-75-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



RN 186668-77-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

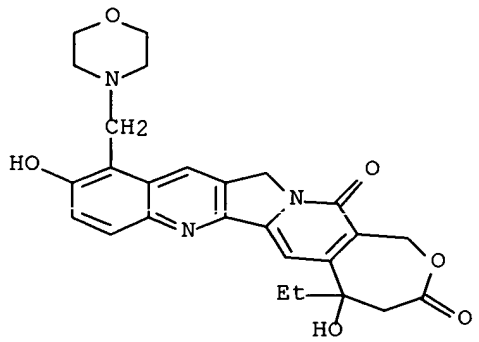


RN 186668-79-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

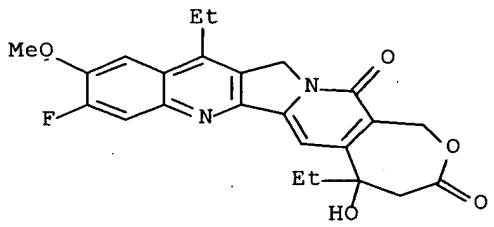


RN 186668-83-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-11-(4-morpholinylmethyl)- (9CI)

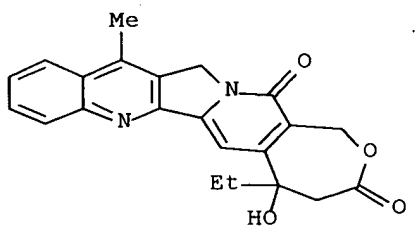
(CA INDEX NAME)



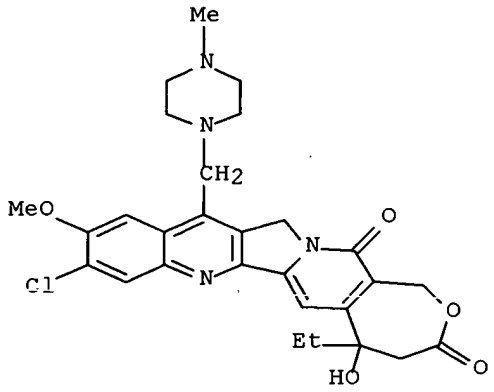
RN 186668-90-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



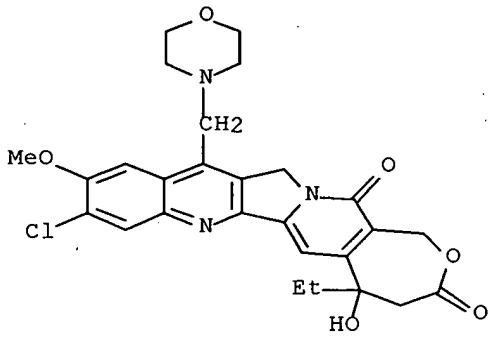
RN 186668-94-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-methyl- (9CI) (CA INDEX NAME)



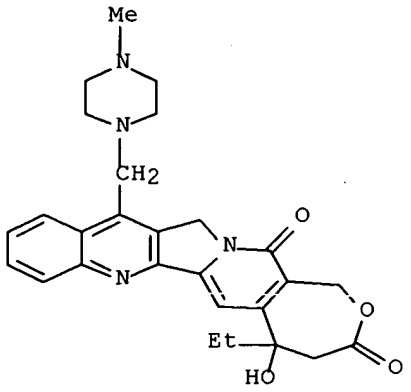
RN 186669-03-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



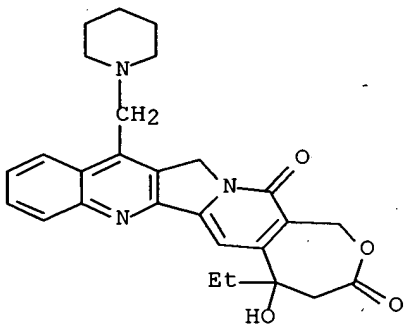
RN 186669-04-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



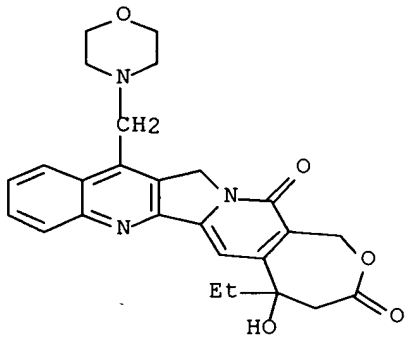
RN 186669-06-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



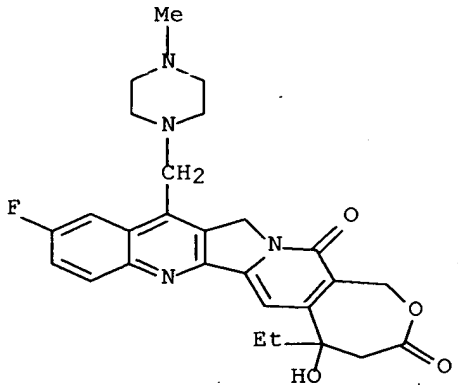
RN 186669-07-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI)
(CA
INDEX NAME)



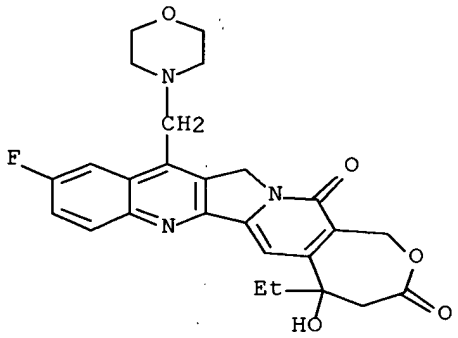
RN 186669-08-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI)
(CA
INDEX NAME)



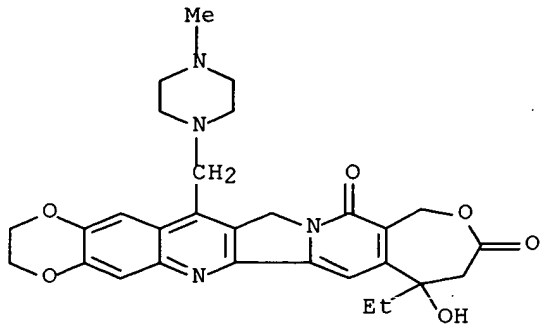
RN 186669-09-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



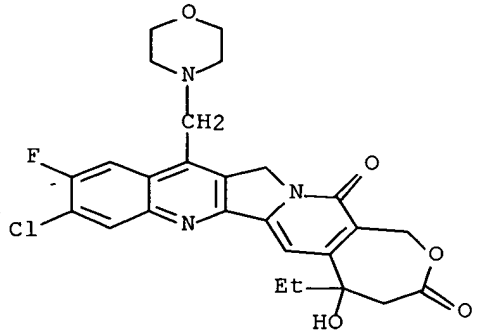
RN 186669-10-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



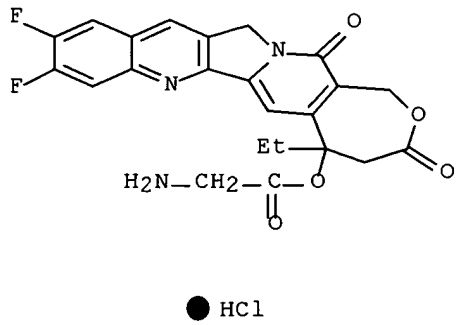
RN 186669-16-9 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy-16-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 186669-18-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)

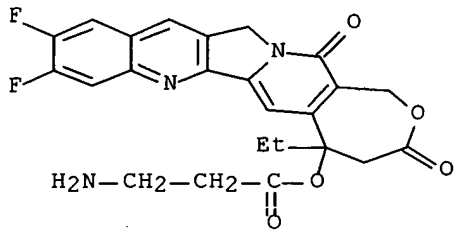


RN 209908-97-4 CAPLUS
CN Glycine, 5-ethyl-9,10-difluoro-4,5,13,15-tetrahydro-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-5-yl ester, monohydrochloride
(9CI) (CA INDEX NAME)

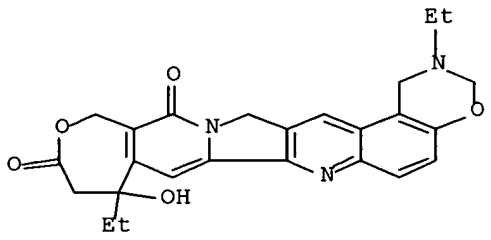


RN 209908-98-5 CAPLUS
CN .beta.-Alanine, 5-ethyl-9,10-difluoro-4,5,13,15-tetrahydro-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-5-yl ester (9CI) (CA

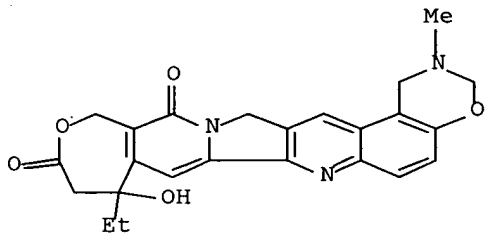
INDEX NAME)



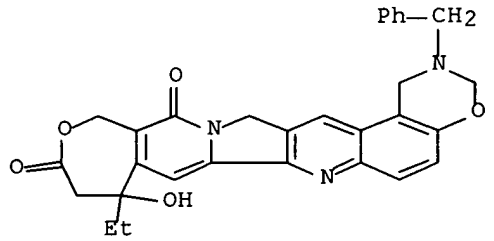
RN 209908-99-6 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 2,9-diethyl-1,2,3,9,10,16-hexahydro-9-hydroxy- (9CI) (CA INDEX NAME)



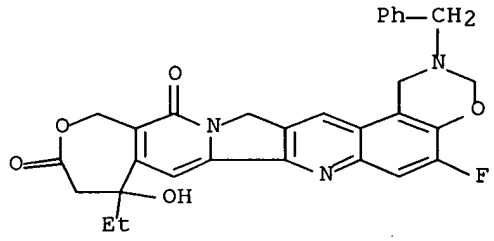
RN 209909-00-2 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 9-ethyl-1,2,3,9,10,16-hexahydro-9-hydroxy-
2-methyl- (9CI) (CA INDEX NAME)



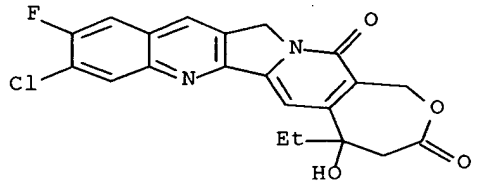
RN 209909-01-3 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 9-ethyl-1,2,3,9,10,16-hexahydro-9-hydroxy-
2-(phenylmethyl)- (9CI) (CA INDEX NAME)



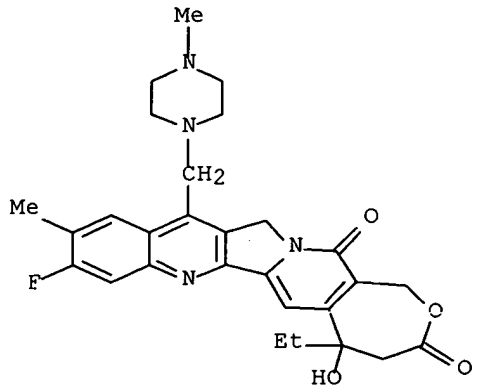
RN 209909-02-4 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 9-ethyl-5-fluoro-1,2,3,9,10,16-hexahydro-9-hydroxy-2-(phenylmethyl)- (9CI) (CA INDEX NAME)



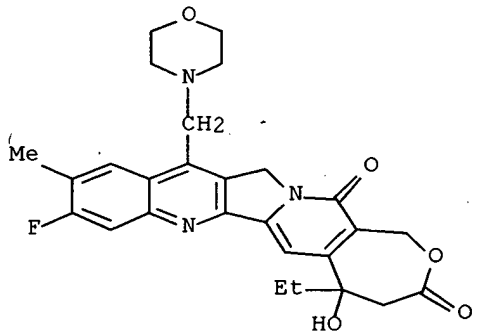
RN 209909-06-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



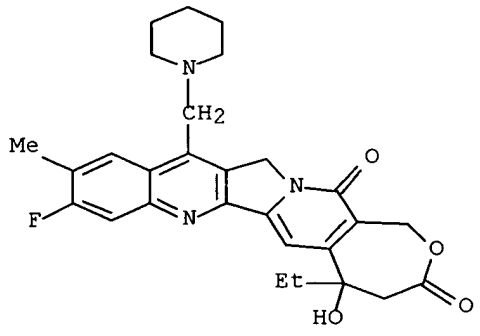
RN 210563-02-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 210563-04-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)

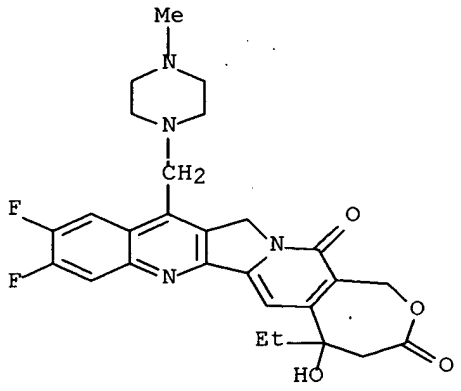


RN 210563-06-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)

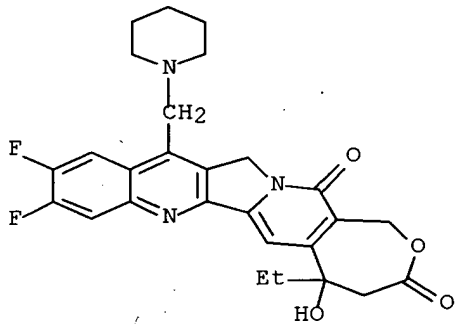


RN 210563-11-4 CAPLUS

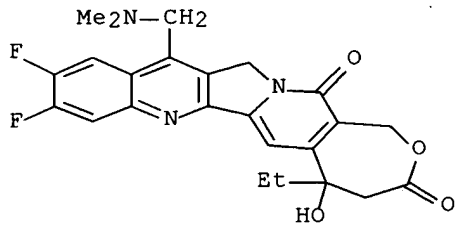
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



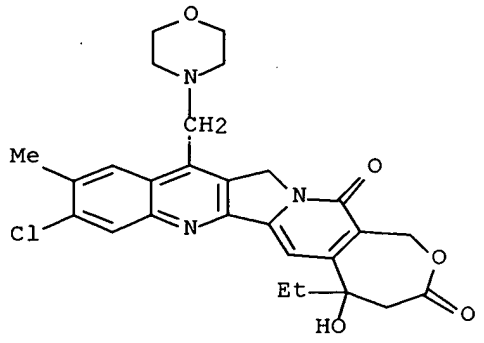
RN 210563-12-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



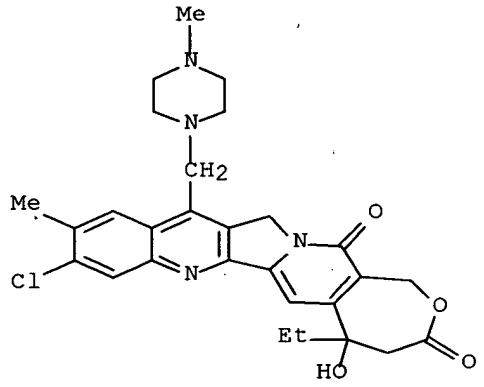
RN 210563-14-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(dimethylamino)methyl]-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



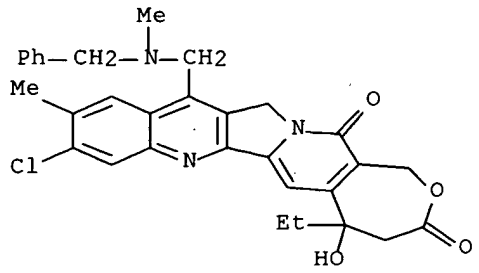
RN 210563-16-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



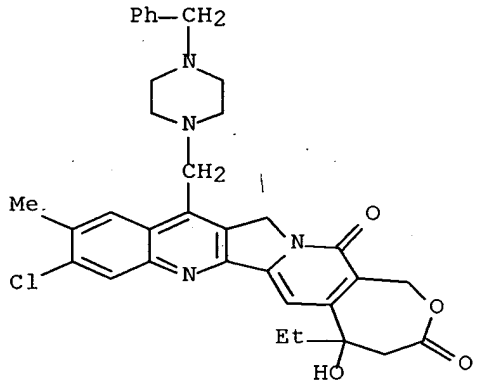
RN 210563-18-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



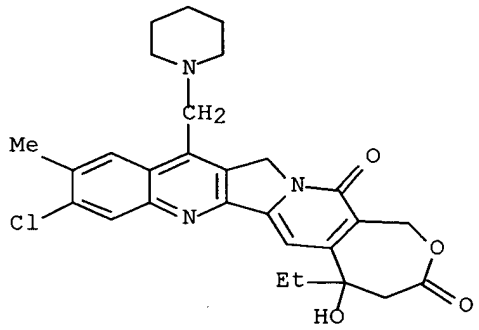
RN 210563-20-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[[methyl(phenylmethyl)amino]methyl]- (9CI) (CA INDEX NAME)



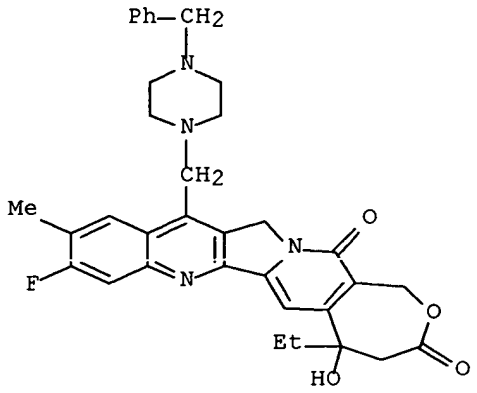
RN 210563-22-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



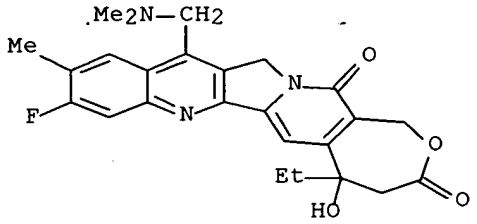
RN 210563-24-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



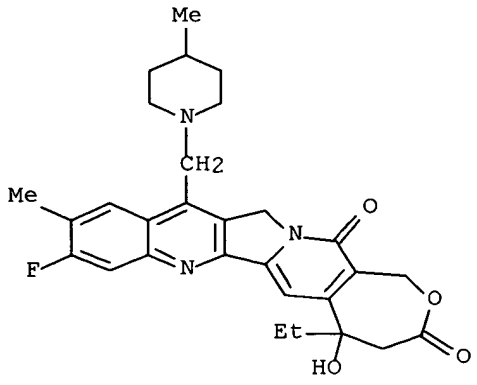
RN 210563-28-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



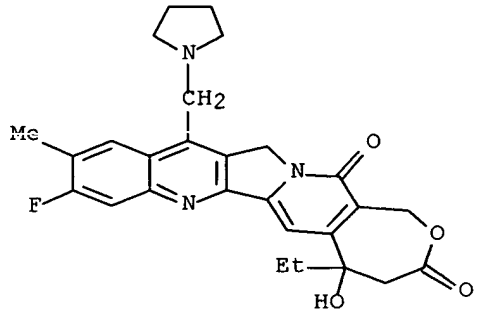
RN 210563-30-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(dimethylamino)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



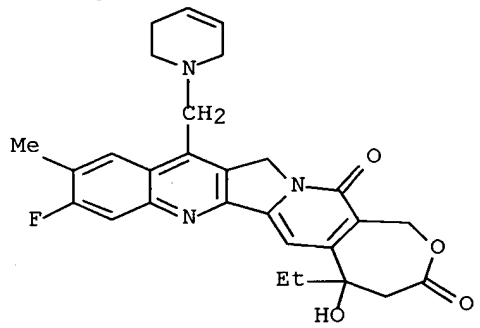
RN 210563-34-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



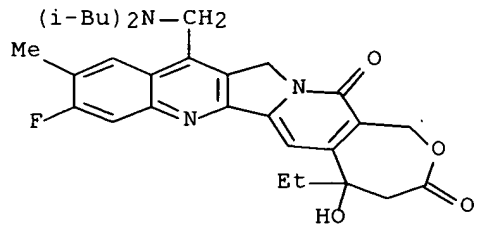
RN 210563-35-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



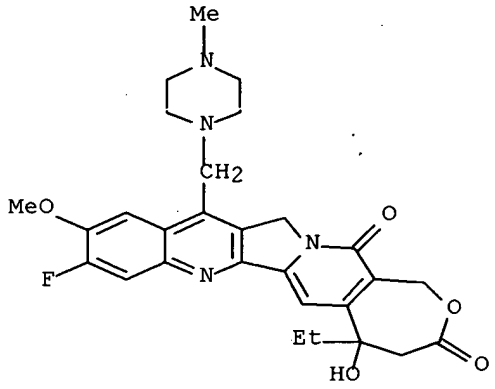
RN 210563-37-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(3,6-dihydro-1(2H)-pyridinyl)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



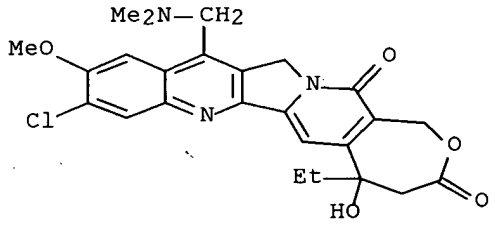
RN 210563-39-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[[bis(2-methylpropyl)amino]methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



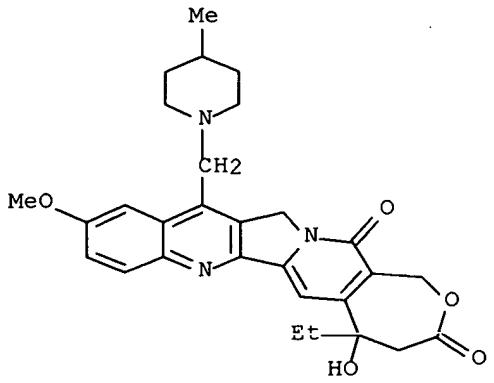
RN 210563-41-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



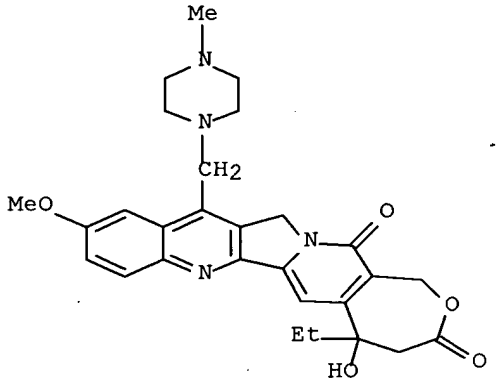
RN 210563-45-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-12-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



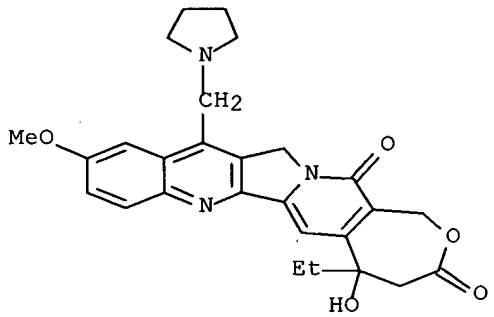
RN 210563-51-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



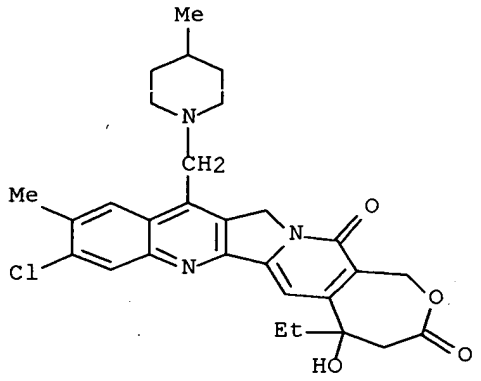
RN 210563-53-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 210563-55-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

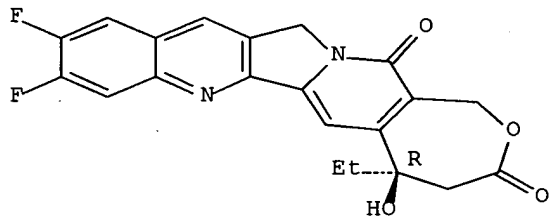


RN 210563-60-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



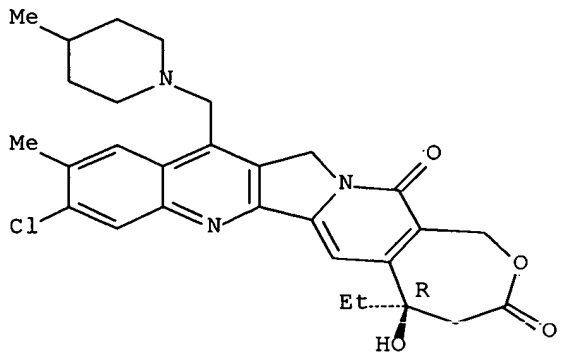
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



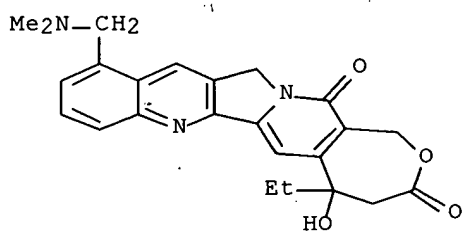
RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



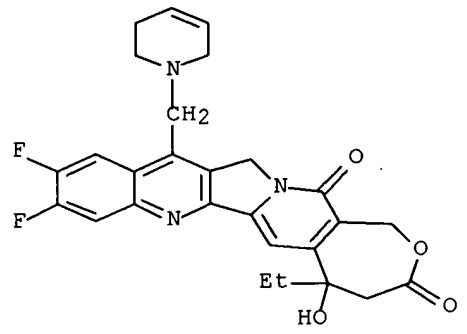
● HCl

RN 387861-24-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)



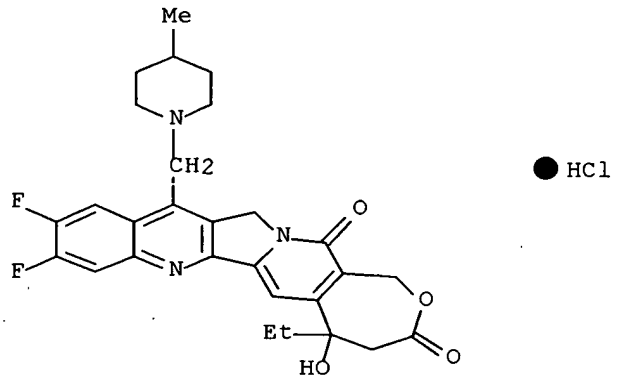
● HCl

RN 387861-59-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(3,6-dihydro-1(2H)-pyridinyl)methyl]-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

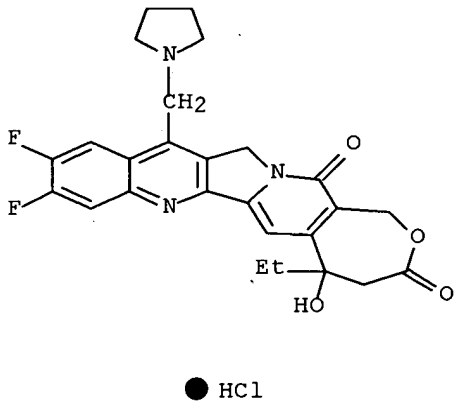


RN 387861-61-2 CAPLUS

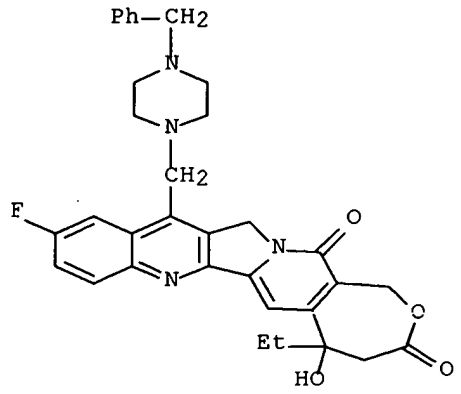
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



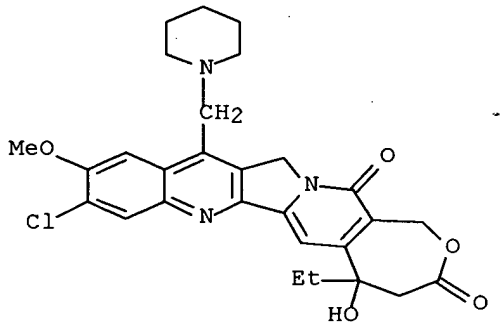
RN 387861-66-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-pyrrolidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



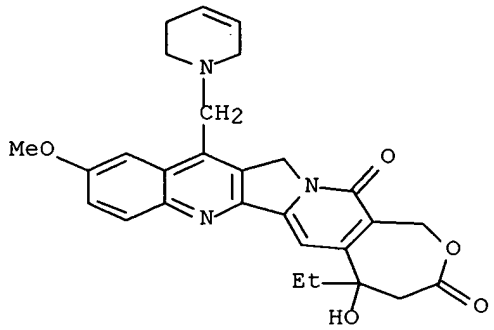
RN 387861-75-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



RN 387861-87-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)

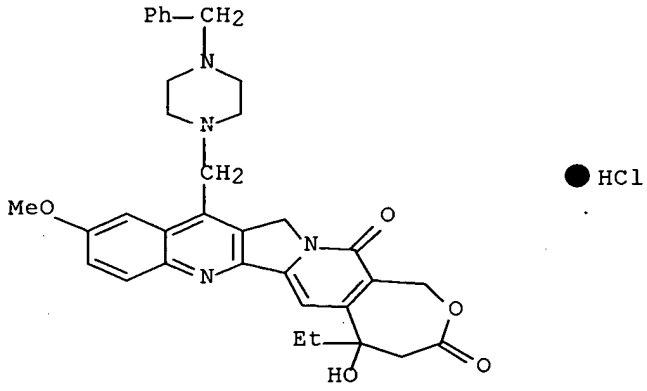


RN 387861-89-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(3,6-dihydro-1(2H)-pyridinyl)methyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)

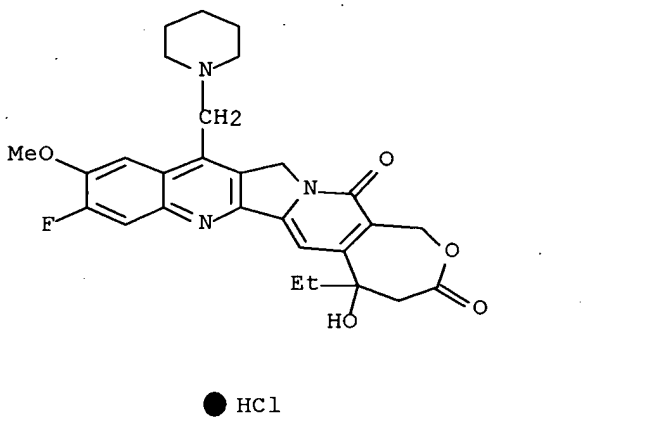


RN 387862-37-5 CAPLUS

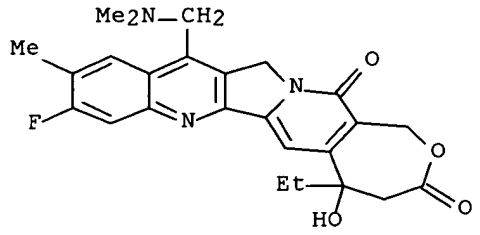
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 387862-83-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-piperidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



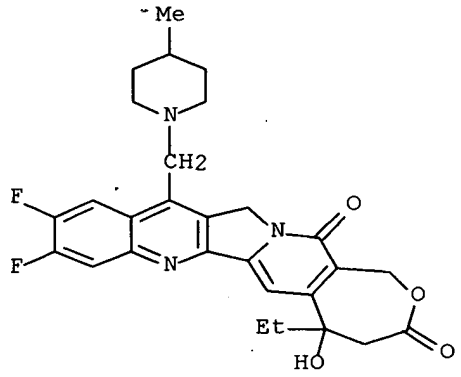
RN 387862-90-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(dimethylamino)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



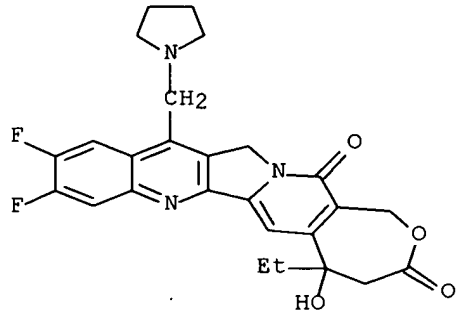
● HCl

IT **210563-08-9P 210563-09-0P 220998-10-7P**
387862-21-7P 387862-39-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents)

RN 210563-08-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)

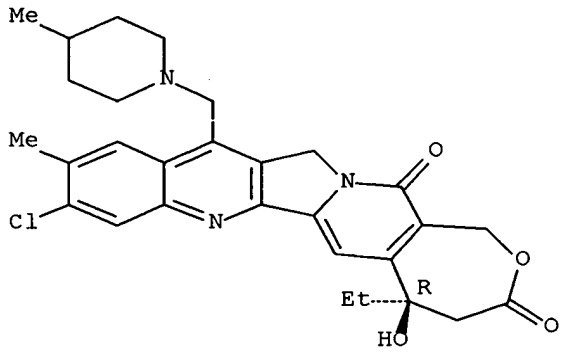


RN 210563-09-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

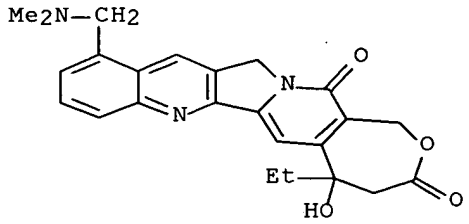


RN 220998-10-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, (5R)- (9CI) (CA INDEX NAME)

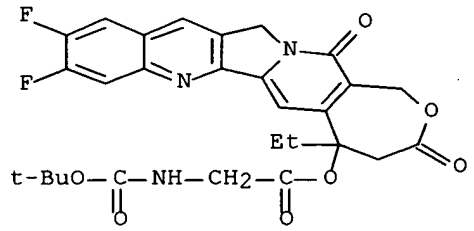
Absolute stereochemistry. Rotation (+).



RN 387862-21-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 387862-39-7 CAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, 5-ethyl-9,10-difluoro-4,5,13,15-tetrahydro-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-5-yl ester (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:906593 CAPLUS
DN 136:226316
TI A novel B-ring modified homocamptothecin, 12-Cl-hCPT, showing antiproliferative and topoisomerase I inhibitory activities superior to SN-38
AU Bailly, Christian; Laine, William; Baldeyrou, Brigitte; Demarquay, Daniele; Huchet, Marion; Coulomb, Helene; Lanco, Christophe; Lavergne, Olivier; Bigg, Dennis C. H.
CS Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, et INSERM U-524, IRCL, Lille, 59045, Fr.
SO Anti-Cancer Drug Design (2001), 16(1), 27-36
CODEN: ACDDEA; ISSN: 0266-9536
PB Oxford University Press
DT Journal
LA English
AB We report the synthesis and pharmacol. evaluation of a novel homocamptothecin (hCPT) deriv., 12-Cl-hCPT, which contains a seven-membered .beta.-hydroxylactone in place of the conventional six-membered .alpha.-hydroxylactone found in camptothecin (CPT) and bears a chloro substituent at position 12. The capacity of 12-Cl-hCPT to inhibit DNA topoisomerase I was compared with that of SN-38, the active metabolite of the clin. used antitumor prodrug CPT-11. In the DNA relaxation assay, 12-Cl-hCPT proved to be slightly more potent than SN-38 at stimulating the formation of nicked plasmid DNA mols. A series of radiolabeled DNA restriction fragments were employed to identify and compare the position of the DNA cleavage sites induced by topoisomerase I in the presence of 12-Cl-hCPT and SN-38. These sequencing studies confirm that both 12-Cl-hCPT and SN-38 strongly promote DNA cleavage by topoisomerase I and reveal that the majority of the cleavage sites are located at the same nucleotide positions for the two drugs. However, a certain no. of DNA cleavage sites were found to be specific to 12-Cl-hCPT. These sites, previously characterized with unsubstituted hCPT, generally correspond to 5'-CG sites whereas the sites common to the 12-Cl-hCPT and SN-38 essentially correspond to 5'-TG sites. We also quantified the formation of drug-induced protein-DNA complexes formed in HT29 human colon carcinoma cells. Trapping of endogenous proteins onto DNA was found to be much more efficient with 12-Cl-hCPT than with SN-38. These data provide a mol. basis to account for the enhanced antiproliferative activity of 12-Cl-hCPT compared with that of SN-38. Biol. evaluation on a panel of sensitive and drug-resistant cell lines revealed 12-Cl-hCPT to be more cytotoxic to tumor cells than SN-38. 12-Cl-hCPT proved 14- and 23-fold more active than SN-38 toward the K562adr and T24anp multidrug-resistant cell lines, resp. The marked topoisomerase I inhibitory properties of 12-Cl-hCPT coupled with its interesting antiproliferative activity, in particular against cancer cells presenting multidrug resistance phenotype with overexpression of P-glycoprotein, makes 12-Cl-hCPT a valid candidate

for subsequent preclin. evaluation. Collectively, the data strengthen homocamptothecin as an extremely promising template to generate novel and potent antitumor agents.

IT **289654-49-5P**

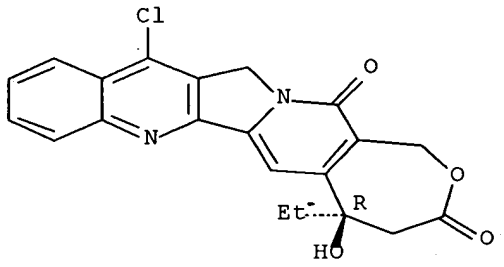
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(novel B-ring modified homocamptothecin, 12-Cl-hCPT, showing antiproliferative and topoisomerase I inhibitory activities superior to SN-38)

RN 289654-49-5 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

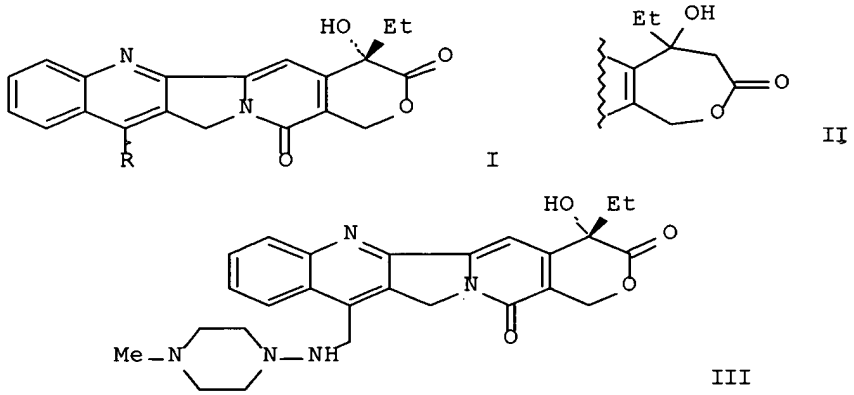


RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:687480 CAPLUS
DN 135:242387
TI Preparation of water-soluble derivatives of camptothecin/homocamptothecin
IN Burke, Thomas G.; Demir, Ayhan S.; Tanyeli, Cihangir; Chavan, Ashok J.; Wang, Tie-Lin; Pommier, Yves
PA University of Kentucky Research Foundation, USA
SO U.S., 36 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

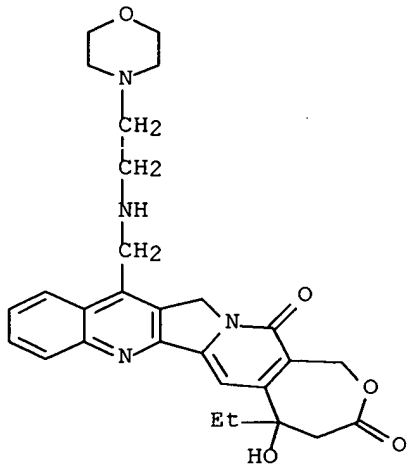
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6291676	B1	20010918	US 2000-517210	20000302
PRAI US 1999-122621P	P	19990303		

OS MARPAT 135:242387
GI

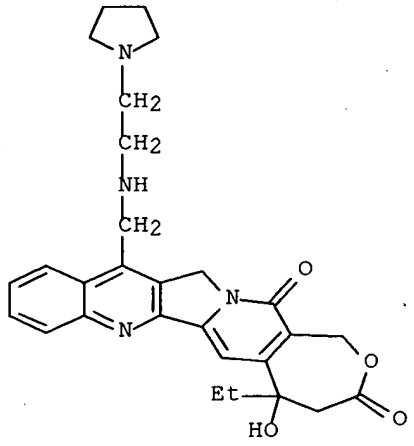


AB Camptothecin and homocamptothecin analogs and derivs. of formulas I and II
[R = (substituted) C1-20 alkyl-NH2] are provided incorporating alkylamine
and polyalkylamine moieties. The compds. have high antitumor activity and
water-soly. and minimal toxicity. Thus, CT-17 (III) was prepd. from camptothecin.
IT **360071-33-6P 360071-34-7P 360071-35-8P**
360071-36-9P 360071-37-0P 360071-38-1P
360071-39-2P 360071-40-5P 360071-41-6P
360071-42-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of water-sol. camptothecin/homocamptothecin derivs.)
RN 360071-33-6 CAPLUS

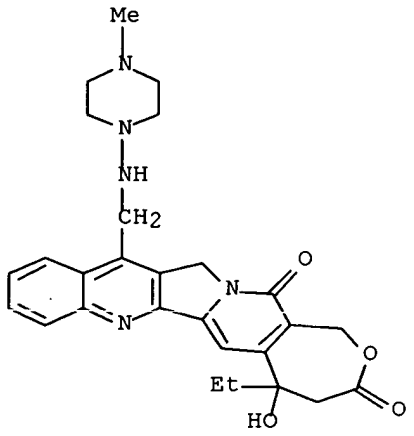
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[[[2-(4-morpholinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)



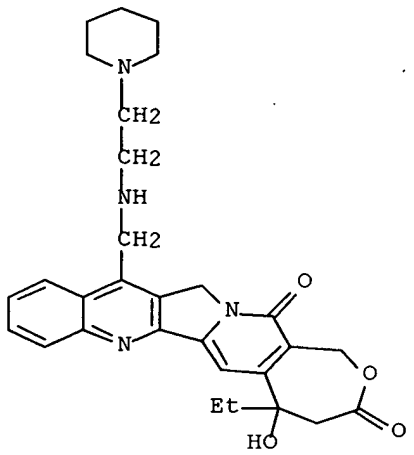
RN 360071-34-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[[[2-(1-pyrrolidinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)



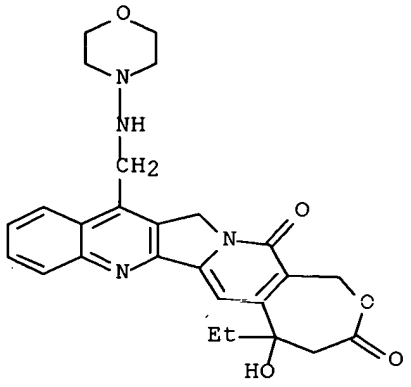
RN 360071-35-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[[(4-methyl-1-piperazinyl)amino]methyl]- (9CI) (CA INDEX NAME)



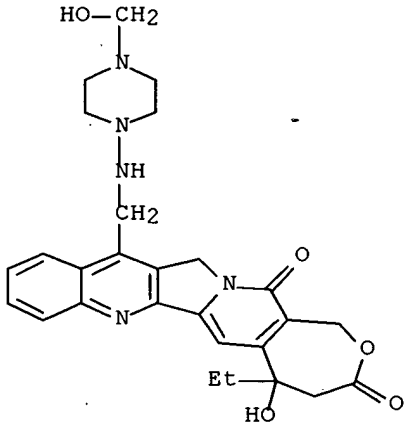
RN 360071-36-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[[[2-(1-piperidinyl)ethyl]amino]methyl]- (9CI) (CA INDEX NAME)



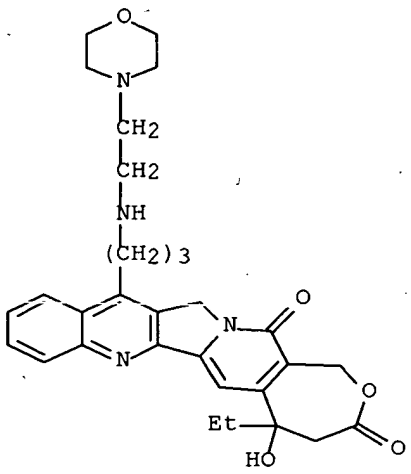
RN 360071-37-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-morpholinylamino)methyl]- (9CI) (CA INDEX NAME)



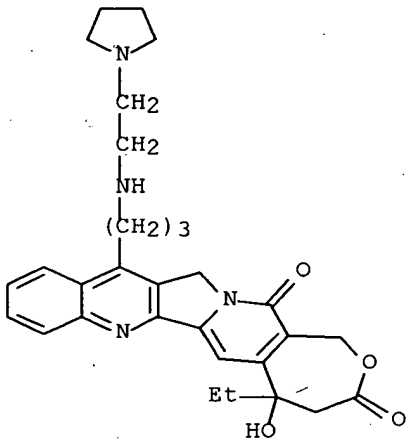
RN 360071-38-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[[[4-(hydroxymethyl)-1-piperazinyl]amino]methyl]- (9CI) (CA INDEX NAME)



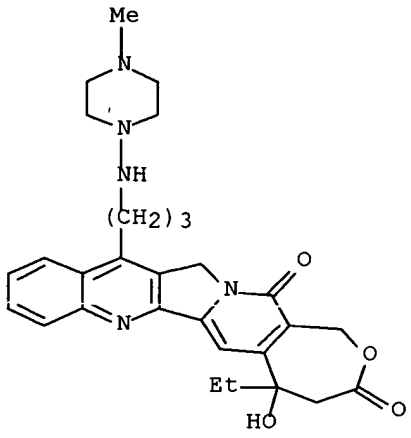
RN 360071-39-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[3-[[2-(4-morpholinyl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)



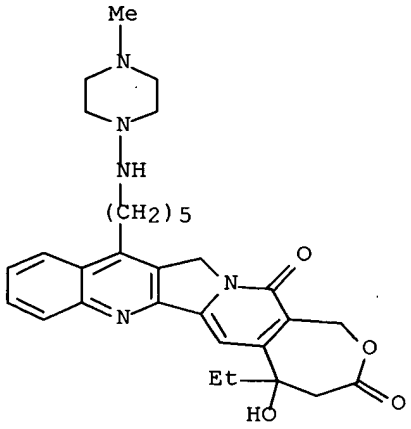
RN 360071-40-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[3-[[2-(1-pyrrolidinyl)ethyl]amino]propyl]- (9CI) (CA INDEX NAME)



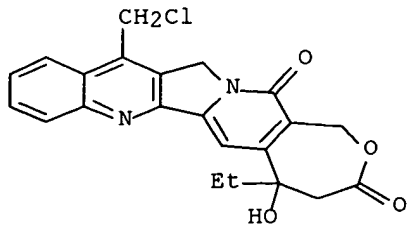
RN 360071-41-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[3-[(4-methyl-1-piperazinyl)amino]propyl]- (9CI) (CA INDEX NAME)



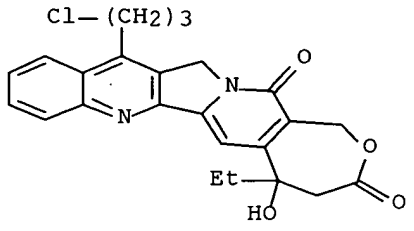
RN 360071-42-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[5-[(4-methyl-1-piperazinyl)amino]pentyl]- (9CI) (CA INDEX NAME)



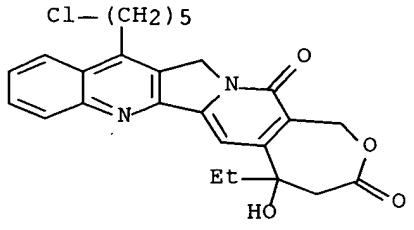
IT **360071-30-3P 360071-31-4P 360071-32-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of water-sol. camptothecin/homocamptothecin derivs.)
RN 360071-30-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(chloromethyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 360071-31-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3-chloropropyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



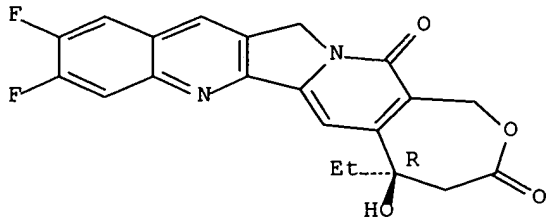
RN 360071-32-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(5-chloropentyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:612480 CAPLUS
DN 135:366413
TI Apoptosis induced by the homocamptothecin anticancer drug BN80915 in HL-60 cells
AU Lansiaux, Amelie; Facompre, Michael; Wattez, Nicole; Hildebrand, Marie-Paule; Bal, Christine; Demarquay, Daniele; Lavergne, Olivier; Bigg, Dennis C. H.; Bailly, Christian
CS Institut National de la Sante et de la Recherche Medicale U-524 and Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, Institut de Recherche sur le Cancer de Lille, Lille, Fr.
SO Molecular Pharmacology (2001), 60(3), 450-461
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB The homocamptothecin (hCPT) deriv. BN80915 contg. a seven-membered Lactone ring represents one of the most potent topoisomerase I inhibitors described. This anticancer agent, currently undergoing phase I clin. trials, has been shown to produce a greater no. of DNA strand breaks than conventional camptothecins with a six-membered lactone ring. To shed light on the mechanism of action of hCPT at the cellular level, we compared the effects of BN80915 and the classic camptothecin SN-38, the active metabolite of irinotecan, on HL-60 human promyelocytic cancer cells. A variety of biochem. events, at both the mitochondrial and the nuclear levels, were characterized to det. how and to what extent the hCPT deriv. can induce apoptotic cell death. The use of cytometry, Western blot anal., confocal microscopy, and different colorimetric assays enabled us to demonstrate that BN80915 is a potent inducer of apoptosis in HL-60 cells. This induction of apoptosis is assocd. with cell cycle changes, a marked decrease of intracellular pH, activation of caspase-3 and -8, DNA fragmentation, and externalization of phosphatidylserine lipids but no significant changes of the mitochondrial membrane potential or the expression of Bcl-2. The interconnections between these different events are discussed. Collectively, the results indicate that the superior activity expressed at the topoisomerase I level leads to a more pronounced induction of apoptosis by BN80915 compared with SN-38. The study identifies and delineates signaling factors involved in BN80915-induced apoptosis in HL-60 cells.
IT **220997-97-7**, BN80915
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(apoptosis induced by homocamptothecin anticancer drug BN80915 in HL-60 cells)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

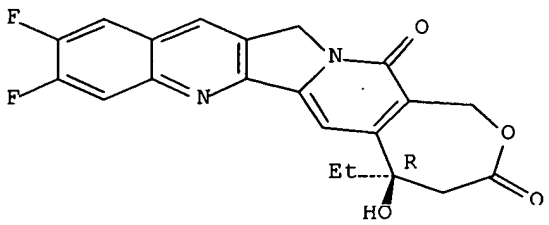


RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:295908 CAPLUS
DN 135:86702
TI Unusual potency of BN 80915, a novel fluorinated E-ring modified camptothecin, toward human colon carcinoma cells
AU Larsen, Annette K.; Gilbert, Cristele; Chyzak, Ginette; Plisov, Sergey Y.; Naguibneva, Irina; Lavergne, Olivier; Lesueur-Ginot, Laurence; Bigg, Dennis C. H.
CS Centre National de la Recherche Scientifique UMR 8532, Institut Gustave-Roussy, Villejuif, F-94805, Fr.
SO Cancer Research (2001), 61(7), 2961-2967
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
AB BN 80915 is the lead compd. from a novel class of E-ring modified camptothecin analogs, the homocamptothecins, which show potent antitumor activities in animal models. Here, we report that BN 80915 induces up to 2-fold more cleavable complexes between plasmid DNA and purified human topoisomerase I than SN-38 and camptothecin. BN 80915 also induces DNA-topoisomerase I complexes in living HT-29 colon carcinoma cells, as shown by the in vivo link assay. BN 80915 is an extremely potent inducer of DNA-protein complexes in these cells starting at a concn. of 5 nM in the media. BN 80915 is clearly more potent than SN-38, because at least 20 times more SN-38 is needed to induce comparable levels of cleavable complexes. Kinetic expts. show that BN 80915 induces cleavable complexes within minutes that remain stable for at least 6 h in the presence of drug. Whereas the majority of the complexes are reversed within 15 min after drug removal, a substantial fraction (30%) persists for at least 4 h, in contrast with SN-38-treated cells, where all complexes have disappeared by this time. BN 80915 shows strong antiproliferative effects toward HT-29 cells with an IC50 of 0.3 nM compared with 20 nM for SN-38 and 40 nM for topotecan. BN 80915 is also potent against other colon carcinoma cells as well as toward cells growing in three dimensions as multicellular spheroids. HL-60 cells expressing functional P-glycoprotein or multidrug resistance protein show no cross-resistance toward BN 80915.
Taken together, our results show that BN 80915 is unusually potent toward human colon carcinoma cells because of the formation of high levels of stable, covalent DNA-topoisomerase complexes.
IT **220997-97-7**, BN 80915
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(potency of BN80915 toward human colon carcinoma cells)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA

INDEX NAME)

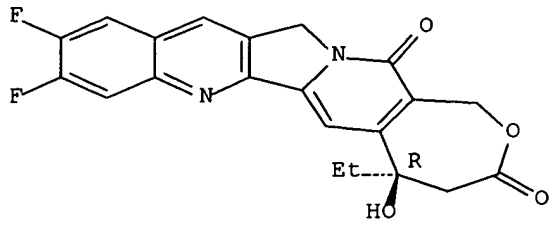
Absolute stereochemistry. Rotation (+).



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

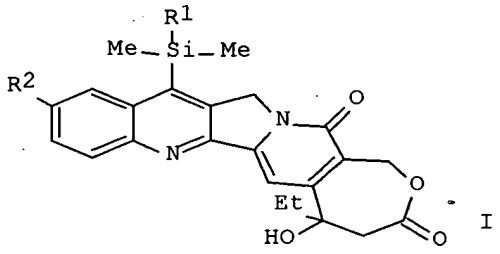
L4 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:125578 CAPLUS
DN 134:348033
TI The homocamptothecin BN 80915 is a highly potent orally active topoisomerase I poison
AU Demarquay, Daniele; Huchet, Marion; Coulomb, Helene; Lesueur-Ginot, Laurence; Lavergne, Olivier; Kasprzyk, Philip G.; Bailly, Christian; Camara, Jose; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Anti-Cancer Drugs (2001), 12(1), 9-19
CODEN: ANTDEV; ISSN: 0959-4973
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB BN 80915, a lead compd. of the homocamptothecin (hCPT) family, has entered clin. trials. BN 80915 is a difluoro-hCPT where the six-membered .alpha.-hydroxylactone ring of camptothecin (CPT) is replaced by a seven-membered .beta.-hydroxylactone ring. Preclin. data reported here show that in spite of the modification to the crucial E-ring of CPTs, BN 80915 retains topoisomerase I poisoning activity as shown in living HT29 cells as well as in cell-free assays, where BN 80915 always performs better than SN-38 or TPT. In antiproliferative assays BN 80915 is also very potent as evidenced by IC50s values consistently lower than those of SN38 in sensitive cell lines as well as in their related multidrug-resistant lines overexpressing P-glycoprotein or multidrug resistance-assocd. protein. Furthermore, in human plasma, in contrast to CPT analogs, the hydrolysis of BN 80915 is slow, leading to improved plasma stability, and irreversible, thus avoiding toxicity related to the accumulation of active principle during excretion in the urinary tract. These findings may account for the good in vivo efficacy obsd. in PC3 xenograft expts. where BN 80915 administered orally at very low doses doubled the tumor growth delay in comparison to CPT-11 administered i.p. Altogether, these results strongly support further development of BN 80915.
IT **220997-97-7**, BN 80915
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecin BN 80915 is a highly potent orally active topoisomerase I poison in treatment of refractory tumors)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

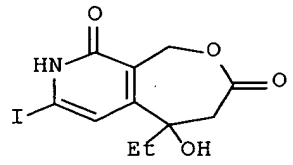
Absolute stereochemistry. Rotation (+).



RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:70498 CAPLUS
DN 134:266468
TI The combinatorial synthesis of racemic homosilatecan libraries via a cascade radical annulation
AU Du, Wu; Gabarda, Ana E.; Bom, David; Curran, Dennis P.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Annals of the New York Academy of Sciences (2000), 922(Camptothecins), 317-319
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
OS CASREACT 134:266468
GI





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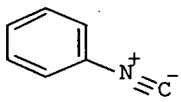
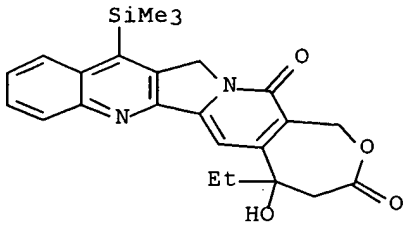


III

AB The authors have developed a practical method for the prepn. of diverse homosilatecan analogs, I (R1 = straight hydrocarbon chain, branched hydrocarbon chain, or aryl group and R2 = H, F, MeO, Me, CF3 or AcO). N-Alkylation of iodopyridone II with different propargyl bromides gave compds. that were subjected to a cascade radical annulation with different aryl isonitriles, e.g. III, to give racemic homosilatecans, e.g. I, with two different elements of diversity. More than 100 racemic homosilatecans were prepd. by this radical annulation reaction by either the traditional way or a Hewlett-Packard soln. phase synthesizer.

IT **300582-87-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(combinatorial synthesis of racemic homosilatecan libraries via a cascade radical annulation)

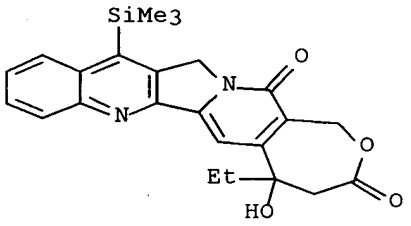
RN 300582-87-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



IT **300582-87-0DP**, C10 hydrogen replaced by fluorine, methoxy, Me, CF3, or acetoxy group and/or one silyl Me group replaced with straight or branched hydrocarbon chain, or aryl group
RL: SPN (Synthetic preparation); PREP (Preparation)
(racemic homosilatecan libraries via a cascade radical annulation)

RN 300582-87-0 CAPLUS

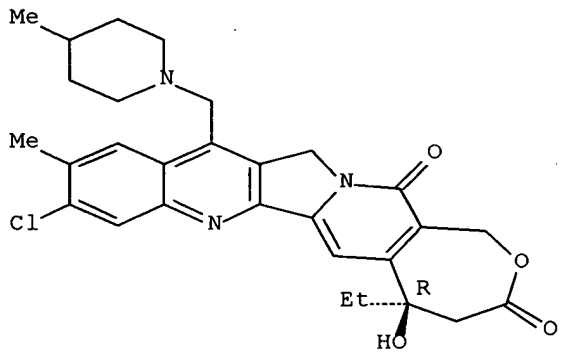
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:70494 CAPLUS
DN 135:86401
TI The dual topoisomerase inhibitor, BN 80927, is highly potent against cell
proliferation and tumor growth
AU Huchet, Marion; Demarquay, Daniele; Coulomb, Helene; Kasprzyk, Philip; Carlson, Mark; Lauer, Jeffrey; Lavergne, Olivier; Bigg, Dennis
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Annals of the New York Academy of Sciences (2000), 922(Camptothecins), 303-305
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal; General Review
LA English
AB A review with 2 refs. focusing on the results of studies on BN 80927 which belongs to a novel family of camptothecin analogs. Findings have shown that the drug is a potent inhibitor of tumor cell proliferation; it shows cytotoxic activity towards resting HT29 cells; and it induces tumor regression in xenograft models.
IT **220997-99-9**, BN 80927
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(dual topoisomerase inhibitor BN 80927 is highly potent against cell proliferation and tumor growth)
RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

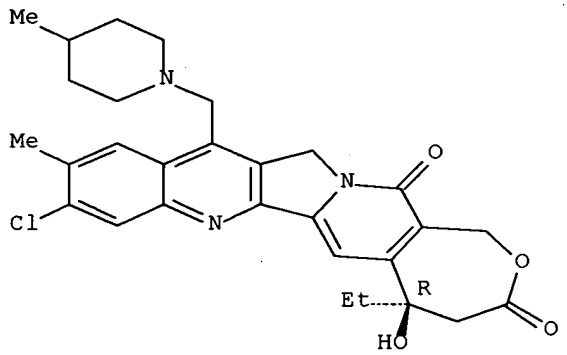


● HCl

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:70493 CAPLUS
DN 135:86664
TI The homocamptothecin, BN 80927, is a potent topoisomerase I poison and topoisomerase II catalytic inhibitor
AU Demarquay, Daniele; Coulomb, Helene; Huchet, Marion; Lesueur-Ginot, Laurence; Camara, Jose; Lavergne, Olivier; Bigg, Dennis
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Annals of the New York Academy of Sciences (2000), 922(Camptothecins), 301-302
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal
LA English
AB Homocamptothecins (hCPTs) represent a new family of camptothecin analogs in which insertion of a methylene spacer between the alc. moiety and carbonyl group of the classical six-membered .alpha.-hydroxylactone ring results in a seven-membered .beta.-hydroxylactone ring which undergoes slow and irreversible hydrolytic ring-opening, providing higher plasma concns. of the active lactone form. Homocamptothecins have been shown to be highly potent antitumor drugs in vitro and in vivo, acting via a classical topoisomerase I poisoning mechanism. Structure activity studies led to the selection of a difluorinated hCPT, BN 80915, which is now in clin. trials. Interestingly, another promising hCPT, BN 80927, which shows inhibitory effects of topoisomerase II activity in addn. to its topoisomerase I poisoning activity, has been discovered. The results are discussed in relation to the antitumor activity of BN 80927.
IT **220997-99-9**, BN 80927
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES(Uses)
RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

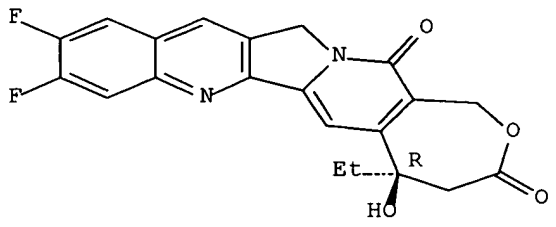


● HCl

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2001:70474 CAPLUS
DN 135:101743
TI Homocamptothecins: E-ring modified CPT analogues
AU Lavergne, Olivier; Demarquay, Daniele; Kasprzyk, Philip G.; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, 91966, Fr.
SO Annals of the New York Academy of Sciences (2000), 922(Camptothecins), 100-111
CODEN: ANYAA9; ISSN: 0077-8923
PB New York Academy of Sciences
DT Journal; General Review
LA English
AB A review with 18 refs. Homocamptothecins (hCPT) are modified camptothecins (CPT) with a seven-membered .beta.-hydroxylactone instead of the naturally occurring six-membered .alpha.-hydroxylactone. This E-ring modification fully conserves the ability to stabilize topo I-DNA single-strand breaks and stimulates high levels of DNA cleavage. A key feature is the irreversibility of E-ring opening, which should give reduced toxicity. Substituted hCPTs have been selected for their high antiproliferative activity on a panel of tumor cell lines, including those with cross resistance, and were active at very low doses in a variety of human tumor xenografts when administered orally. BN 80915, a difluoro-hCPT, has entered clin. trials.
IT **220997-97-7**, BN 80915
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecins: E-ring modified CPT analogs)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



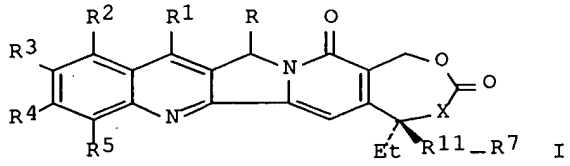
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2000:790315 CAPLUS
DN 133:350387
TI Synthesis of novel highly lipophilic camptothecin analogs for use in treating cancers and leukemia
IN Kochat, Harry; Chen, Xinghai; Huang, Qiuli; Peddaiaghari, Seetharamulu; Hausheer, Frederick H.
PA Bionumerik Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066127	A1	20001109	WO 2000-US12318	20000504

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-132414P P 19990504
OS MARPAT 133:350387
GI



I

AB This invention discloses the prepn. of novel analogs of camptothecin {I; R, R1 = H, alkyl, alkenyl, alkynyl, alkoxy, halo, aryl, arylalkyl, arylalkenyl, arylalkynyl, -X1-(alkylene, alkenylene, alkynylene)-SiR12R13R14 (R12 = R13 = R14 = H, alkyl), -X1-(alkylene, alkenylene, alkynylene, phenylene, benzylene)-NR9R10 (R9, R10 = H, alkyl or nitrogen protecting group), OR6 (R6 = H, alkyl or oxygen protecting group); R2 = R3 = R4 = R5 = H, alkyl, alkenyl, alkynyl, alkoxy, halo, aryl, arylalkyl, arylalkenyl, arylalkynyl, amino, protected amino, nitro, -X2-(alkylene, alkenylene, alkynylene)-SiR12R13R14, -X2-(alkylene, alkenylene, alkynylene, phenylene, benzylene)-NR9R10 [X1, X2 = individually S, NR15(R15 = H, alkyl, N-protecting group or absent)], or OR8 [R8 = H, alkyl or -(alkylene, alkenylene or alkynylene)-SiR12R13R14]; R7 = H, alkyl, aryl, -SiR12R13R14 or absent when R11 = H; R11 = H, CO, SO2, CS, SO, alkylene, O or S; X = CH2 or absent} or a pharmaceutically acceptable salt

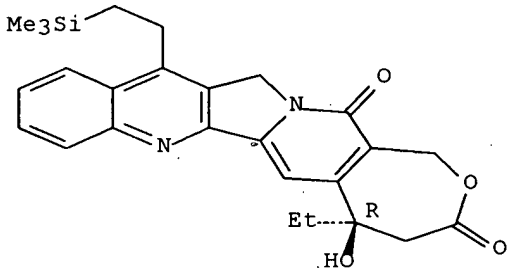
thereof. Thus, I (R = R2 = R3 = R4 = R5 = R7 = H, R1 = CH2CH2Si(Me)3, R11
= O, X = CH2) (II) was prepd. by the reaction of homocamptothecin I [R = R1 = R2 = R3 = R4 = R5 = R7 = H, R11 = O, X = CH2(III)] with 3-trimethylsilyl-propanal.

IT **289653-95-8P**, 7-Trimethylsilylethyl homocamptothecin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(Synthesis of novel highly lipophilic camptothecin analogs for use in treating cancers and leukemia)

RN 289653-95-8 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

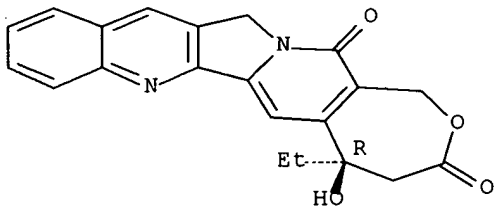


IT **186669-19-2P**, E-Homocamptothecine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Synthesis of novel highly lipophilic camptothecin analogs for use in treating cancers and leukemia)

RN 186669-19-2 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2000:741925 CAPLUS
DN 133:296587
TI Preparation of camptothecin analogs for pharmaceutical use in the treatment of cancer
IN Curran, Dennis P.; Bom, David; Burke, Thomas G.
PA University of Pittsburgh, USA; University of Kentucky Research Foundation
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000061146	A1	20001019	WO 2000-US9401	20000407
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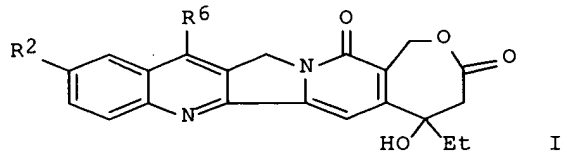
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6207832	B1	20010327	US 1999-290019	19990409
	EP 1173180	A1	20020123	EP 2000-921919	20000407
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002541201	T2	20021203	JP 2000-610479	20000407
	US 2001003779	A1	20010614	US 2000-728031	20001130
	US 6410731	B2	20020625		
PRAI	US 1999-290019	A	19990409		
	WO 2000-US9401	W	20000407		

OS MARPAT 133:296587
GI



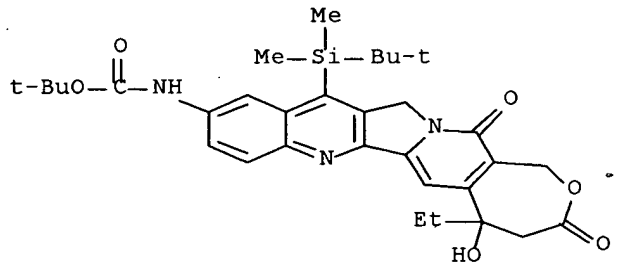
I

AB Camptothecin analogs, such as I [R2 = H, OH, NH2, acyl, alkoxy, acyloxy, etc.; R6 = silyl, silylalkyl, silylalkenyl, silylalkynyl, etc.], were prepd. for use as antitumor agents. Thus, (.+-.)-10-amino-7-(tert-butyldimethylsilyl)homocamptothecin, a.k.a. DB 90, was prepd. via a multistep synthetic sequence starting from 4-ethyl-8-methoxy-6-(trimethylsilyl)-1H-pyrano[3,4-c]pyridine, tert-Bu bromoacetate, 1-bromo-3-tert-butyldimethylsilyl-2-propyne, and 4-(tert-Butyloxycabonylamino)phenylisocyanate. The prepd. homocamptothecins

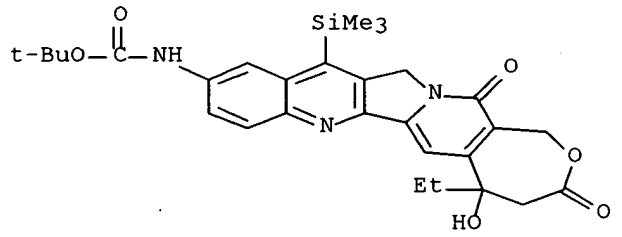
were
tested for activity against MDA-MB-435 tumorigenic metastatic human breast
cancer cells.

IT **300582-81-4P 300582-89-2P 300582-92-7P**
300582-93-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(prepn. of camptothecin analogs for pharmaceutical use in the treatment
of cancer)

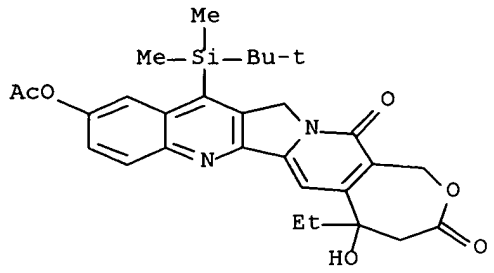
RN 300582-81-4 CAPLUS
CN Carbamic acid, [12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



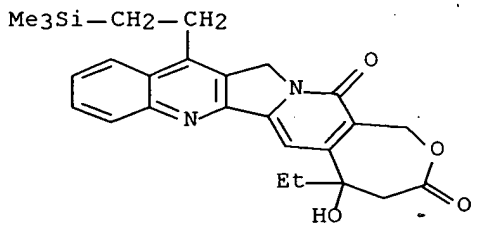
RN 300582-89-2 CAPLUS
CN Carbamic acid, [5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-12-(trimethylsilyl)-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-10-yl]-
, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



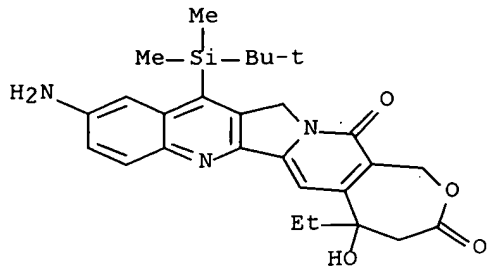
RN 300582-92-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



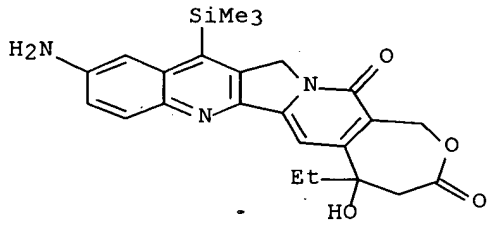
RN 300582-93-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]-(9CI)
(CA INDEX NAME)



IT **247043-96-5P**, Camptothecin DB 90 **247043-97-6P**, DB 38
247043-98-7P, DB 91 **247043-99-8P**, DB 81
300582-87-0P 300582-91-6P 300582-94-9P
300582-96-1P 300582-98-3P 300582-99-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs for pharmaceutical use in the treatment of cancer)
RN 247043-96-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

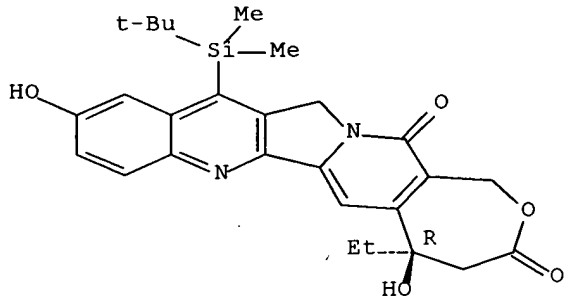


RN 247043-97-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)-(9CI)
(CA INDEX NAME)

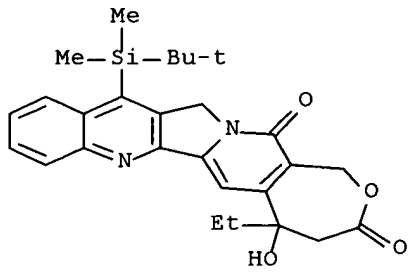


RN 247043-98-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, (5R)- (9CI) (CA INDEX NAME)

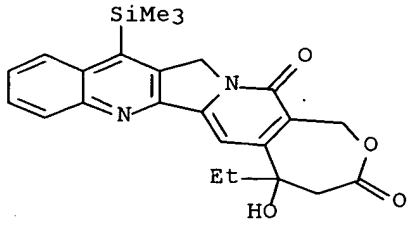
Absolute stereochemistry. Rotation (+).



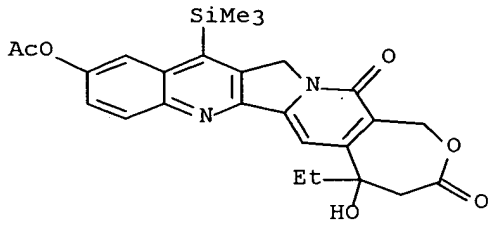
RN 247043-99-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



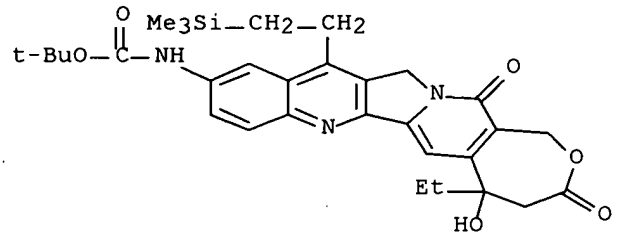
RN 300582-87-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)- (9CI) (CA INDEX NAME)



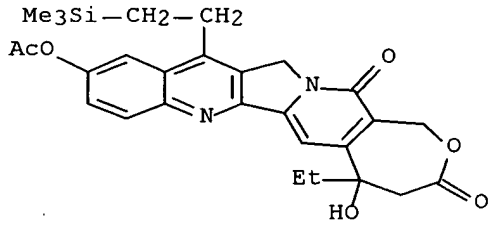
RN 300582-91-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)-
(9CI) (CA INDEX NAME)



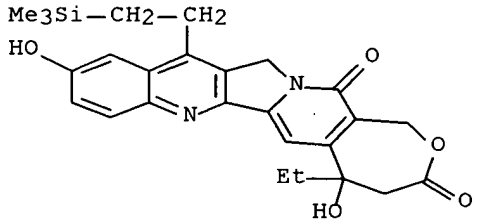
RN 300582-94-9 CAPLUS
CN Carbamic acid, [5-ethyl-4,5,13,15-tetrahydro-5-hydroxy-3,15-dioxo-12-[2-(trimethylsilyl)ethyl]-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-
10-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



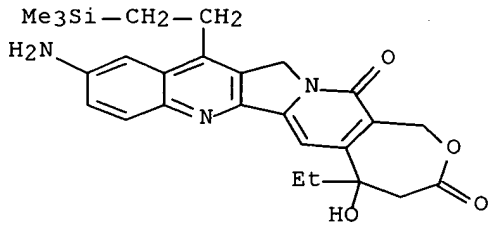
RN 300582-96-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-(acetyloxy)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



RN 300582-98-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



RN 300582-99-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]- (9CI) (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

Current App

L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2000:608751 CAPLUS
DN 133:193314
TI Preparation of optically pure camptothecin analogs for pharmaceutical use as anticancer agents
IN Lavergne, Olivier; Bigg, Dennis; Lanco, Christophe; Rolland, Alain
PA Societe de Conseils de Recherches et d'applications Scientifiques (S.C.R.A.S, Fr.
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050427	A1	20000831	WO 2000-FR461	20000224
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2790261	A1	20000901	FR 1999-2398	19990226
	NZ 514153	A	20010928	NZ 2000-514153	20000224
	EP 1165565	A1	20020102	EP 2000-907714	20000224
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	BR 2000008526	A	20020108	BR 2000-8526	20000224
	JP 2002537399	T2	20021105	JP 2000-601007	20000224
	NO 2001004117	A	20011011	NO 2001-4117	20010824
	US 2003004150	A1	20030102	US 2002-71046	20020206
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	GB 1995-12670	A	19950621		
	WO 1996-FR980	W	19960621		
	FR 1996-15774	A	19961220		
	FR 1996-15775	A	19961220		
	FR 1996-15945	A	19961224		
	FR 1997-10785	A	19970829		
	US 1997-973561	A2	19971202		
	WO 1997-FR2217	W	19971205		
	WO 1997-FR2218	W	19971205		
	WO 1998-FR1768	W	19980807		
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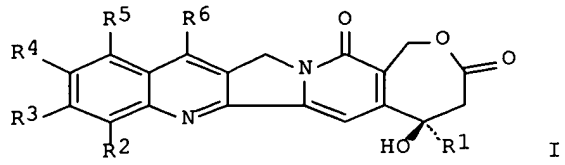


I

AB Camptothecin analogs I [R1 = alkyl; R2-5 = H, halogen, sulfonyloxy; R6 = H, Ph, alkyl, hydroxyalkyl, cycloalkyl, substituted alkyl, aryl, etc.] with topoisomerase inhibiting activity were prepd. for use as antitumor agents. Thus, I (R1 = Et, R5 = F, R2 = R3 = R4 = R6 = H) was prepd. by a multistep synthetic sequence starting from .beta.-ethyl-.beta.-hydroxy-2-methoxy-3-[(phenylmethoxy)methyl]-4-pyridinepropanoic acid 1,1-dimethylethyl ester, 2-amino-6-fluorobenzoic acid, and Et malonyl chloride. The prepd. camptothecin analogs were tested for inhibition of cell proliferation of HT29 human colon adenocarcinoma cells.

IT **284684-29-3P**

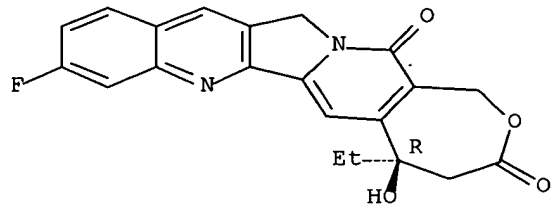
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of optically pure camptothecin analogs for pharmaceutical use as anticancer agents)

RN 284684-29-3 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **284684-27-1P 284684-31-7P 284684-32-8P**
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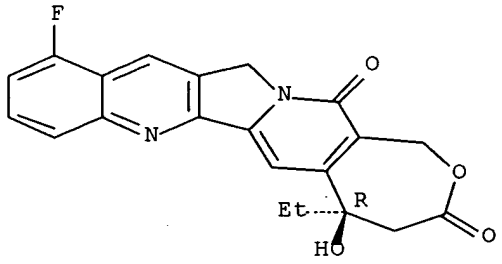
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of optically pure camptothecin analogs for pharmaceutical use as anticancer agents)

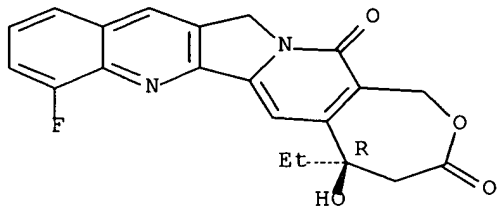
RN 284684-27-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-11-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



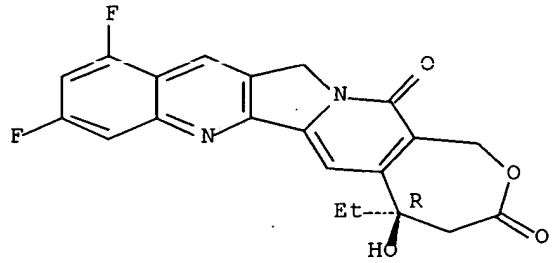
RN 284684-31-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-8-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



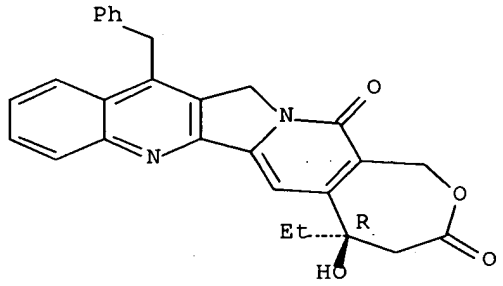
RN 284684-32-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



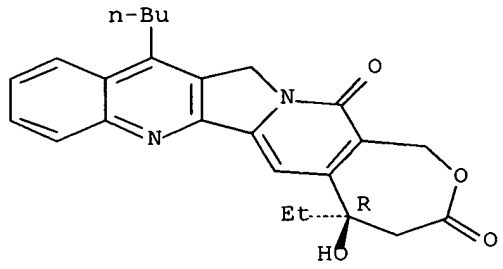
RN 289653-65-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(phenylmethyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



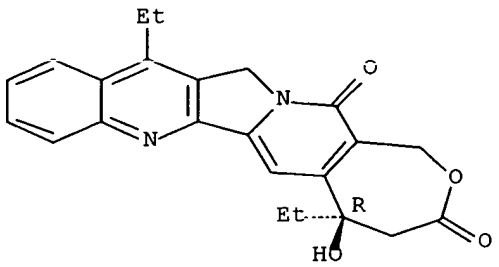
RN 289653-67-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-butyl-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



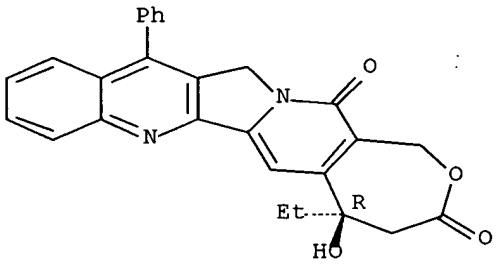
RN 289653-68-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



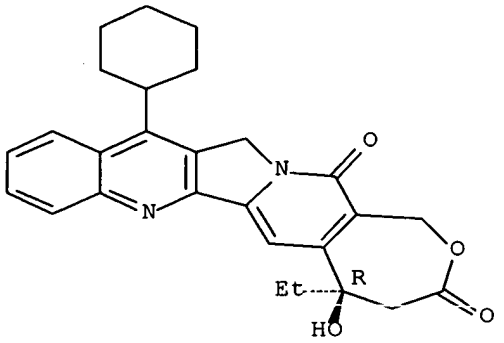
RN 289653-70-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-phenyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



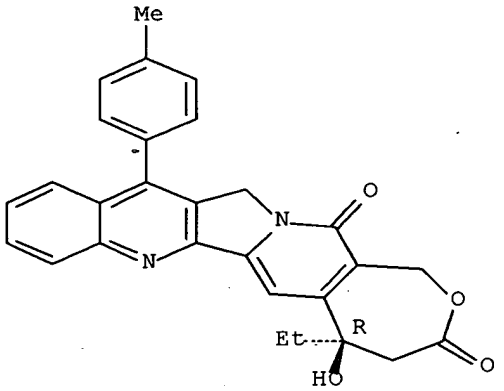
RN 289653-72-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-cyclohexyl-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



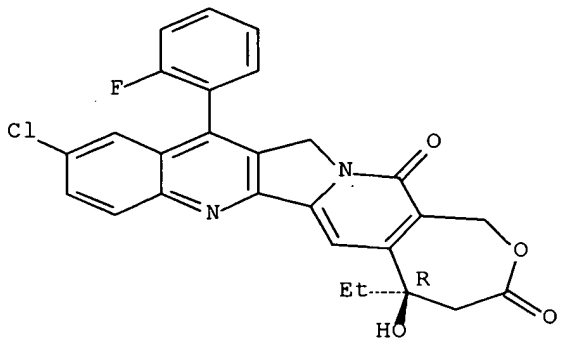
RN 289653-74-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(4-methylphenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



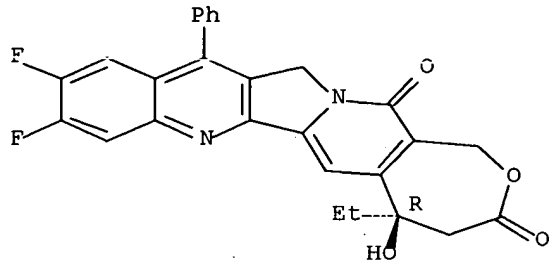
RN 289653-76-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-12-(2-fluorophenyl)-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



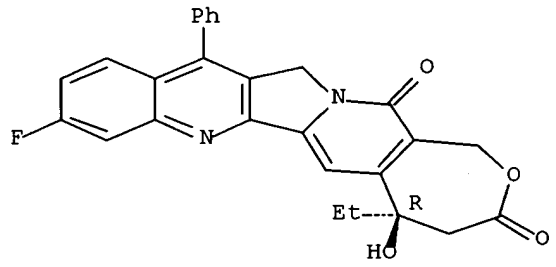
RN 289653-78-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-phenyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



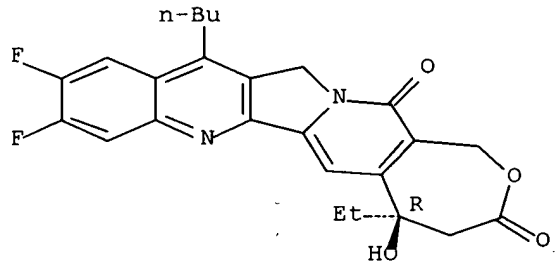
RN 289653-79-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-phenyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



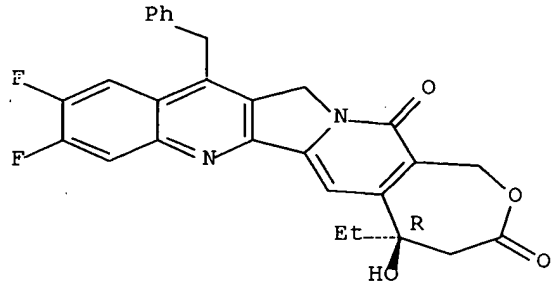
RN 289653-81-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-butyl-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



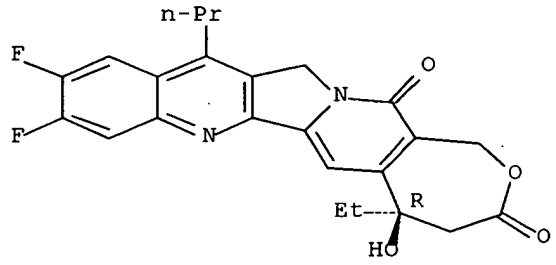
RN 289653-83-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(phenylmethyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



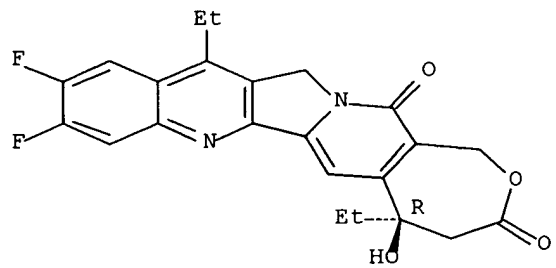
RN 289653-84-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-propyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



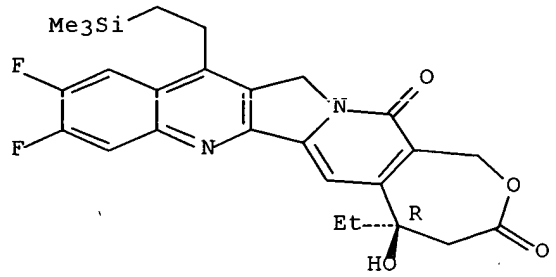
RN 289653-86-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



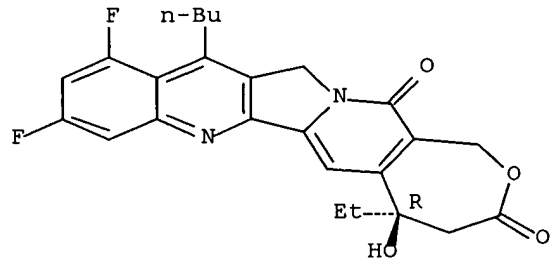
RN 289653-88-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



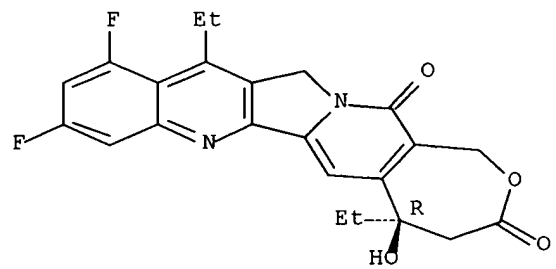
RN 289653-90-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-butyl-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



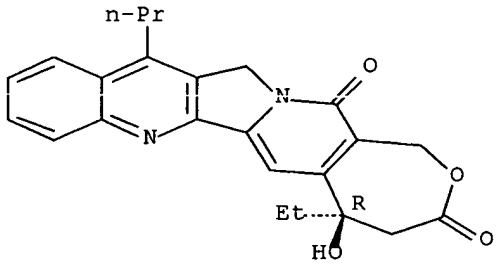
RN 289653-91-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



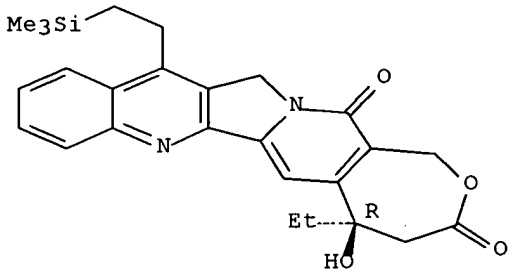
RN 289653-93-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-propyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



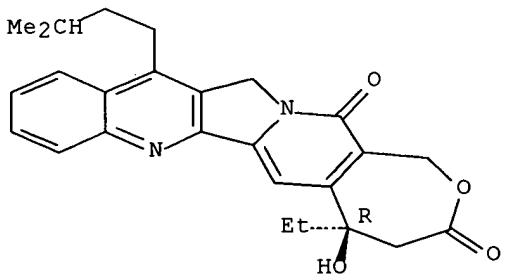
RN 289653-95-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[2-(trimethylsilyl)ethyl]-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



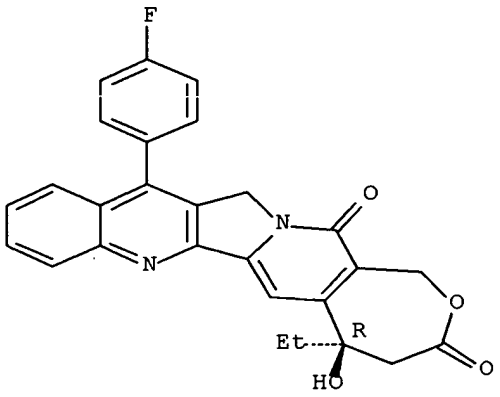
RN 289653-96-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(3-methylbutyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



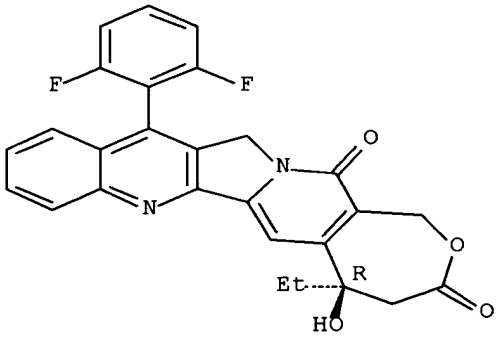
RN 289653-97-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-12-(4-fluorophenyl)-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



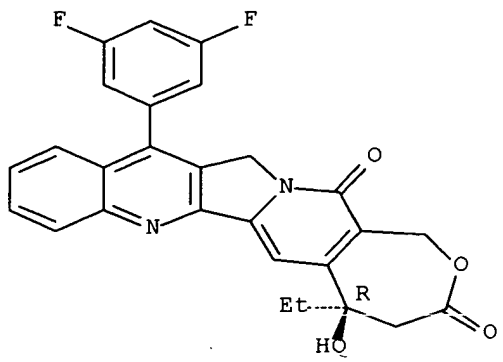
RN 289653-98-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2,6-difluorophenyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



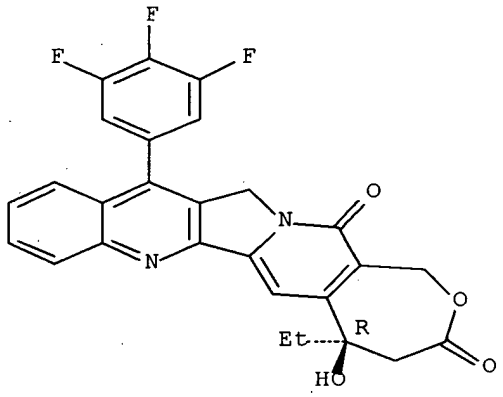
RN 289653-99-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,5-difluorophenyl)-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



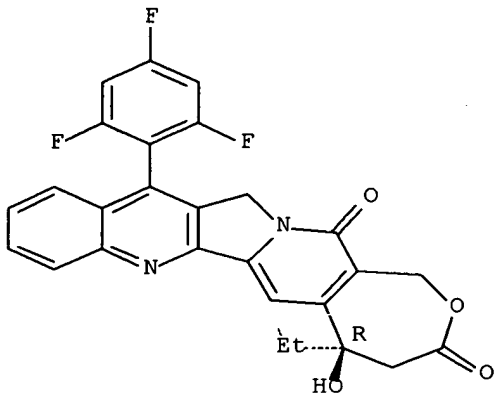
RN 289654-00-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(3,4,5-trifluorophenyl)-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



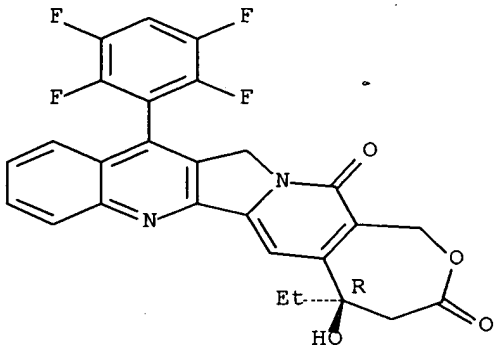
RN 289654-01-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(2,4,6-trifluorophenyl)-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



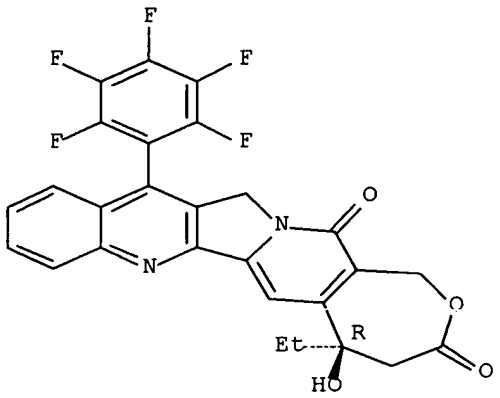
RN 289654-02-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(2,3,5,6-tetrafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



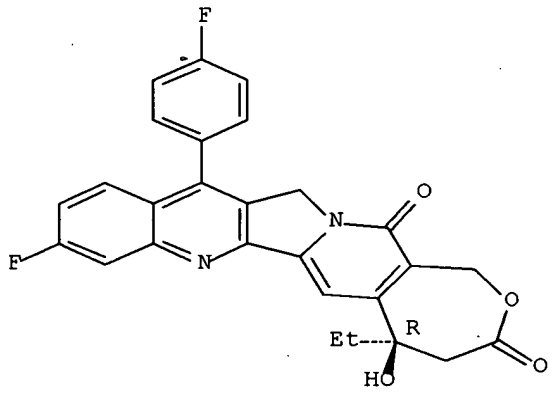
RN 289654-03-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(pentafluorophenyl)-, (5R)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



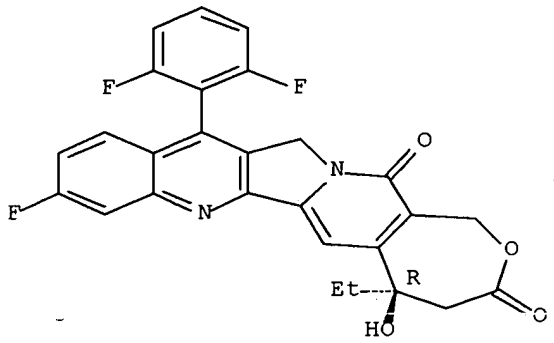
RN 289654-04-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-12-(4-fluorophenyl)-1,4,5,13-tetrahydro-5-hydroxy-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



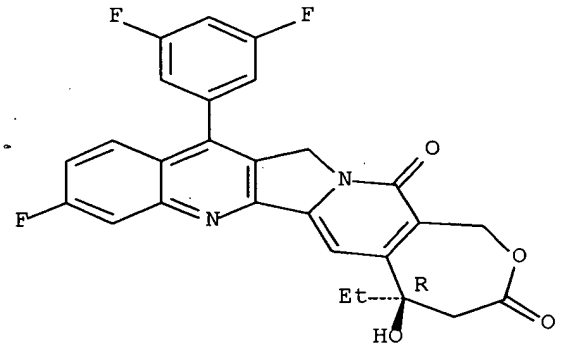
RN 289654-05-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2,6-difluorophenyl)-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



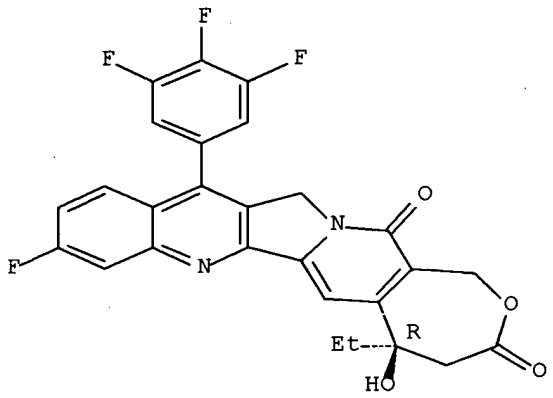
RN 289654-06-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,5-difluorophenyl)-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



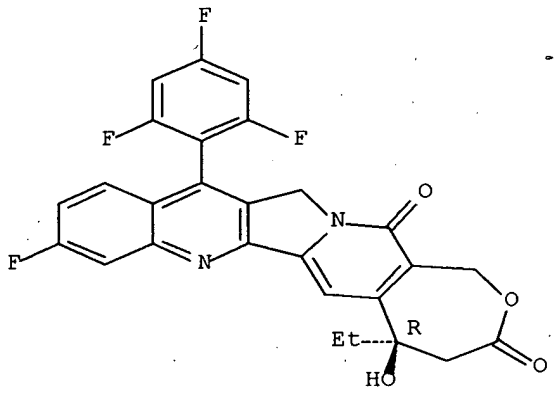
RN 289654-07-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3,4,5-trifluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



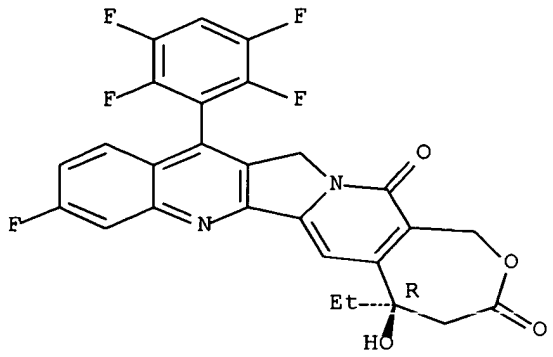
RN 289654-08-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2,4,6-trifluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



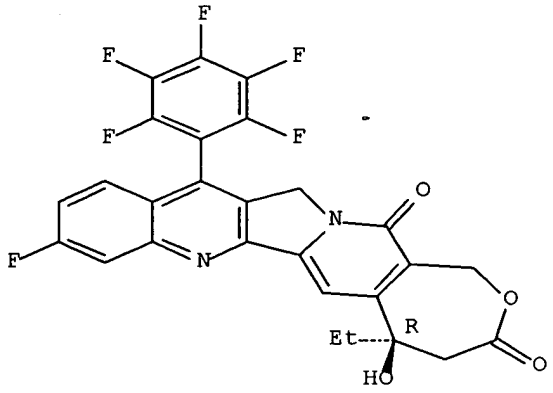
RN 289654-09-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2,3,5,6-tetrafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



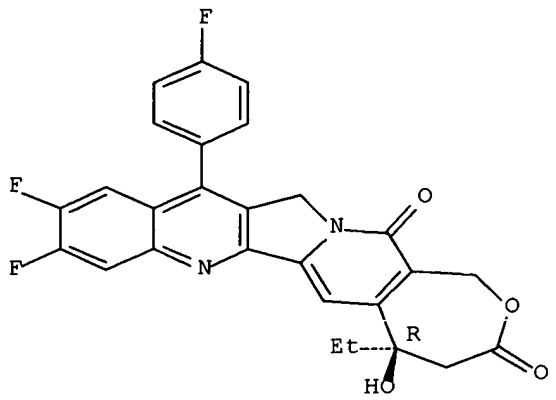
RN 289654-10-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(pentafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



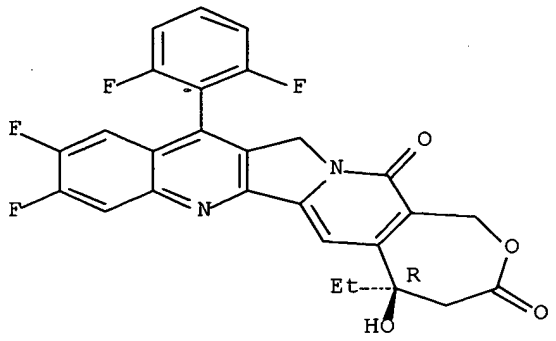
RN 289654-11-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-12-(4-fluorophenyl)-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



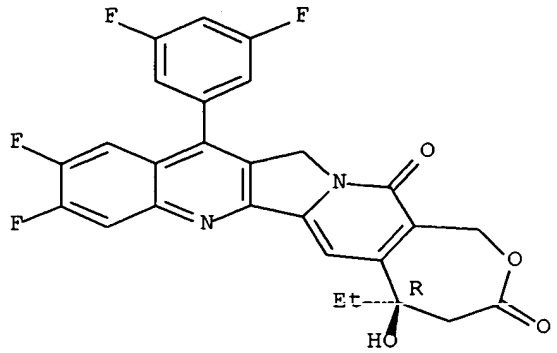
RN 289654-12-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2,6-difluorophenyl)-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



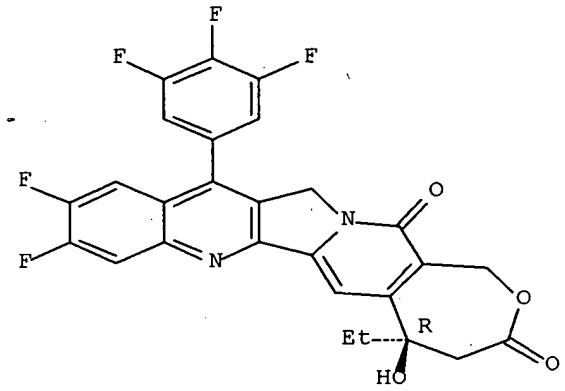
RN 289654-13-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,5-difluorophenyl)-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



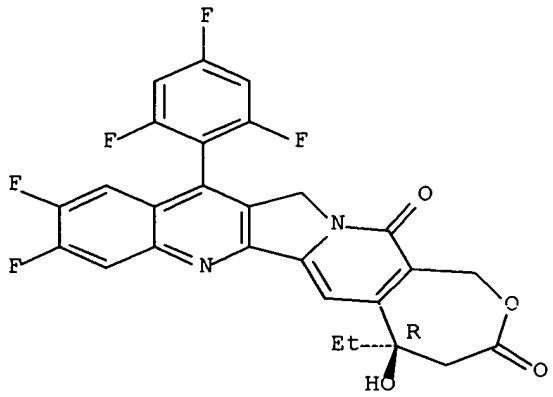
RN 289654-14-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3,4,5-trifluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



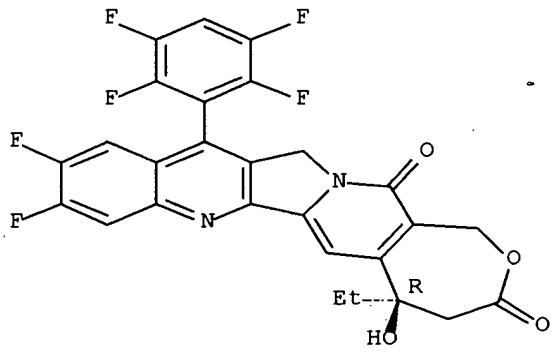
RN 289654-15-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2,4,6-trifluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



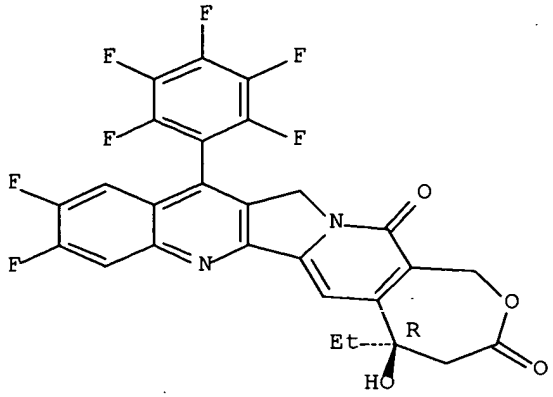
RN 289654-16-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2,3,5,6-tetrafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



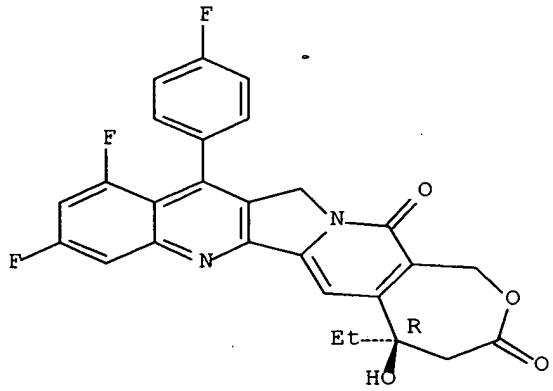
RN 289654-17-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(pentafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



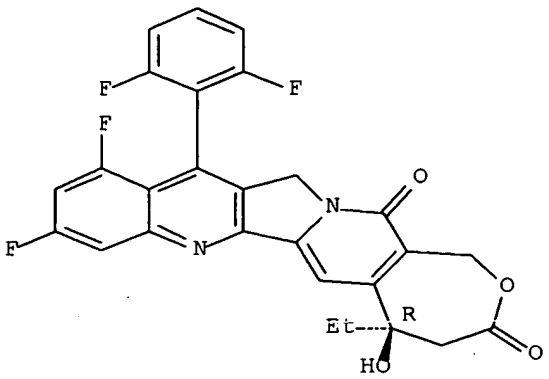
RN 289654-18-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-12-(4-fluorophenyl)-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



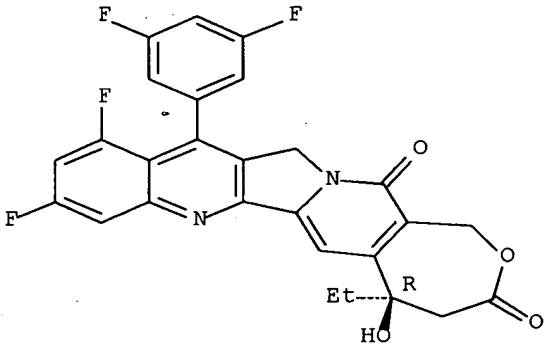
RN 289654-19-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2,6-difluorophenyl)-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



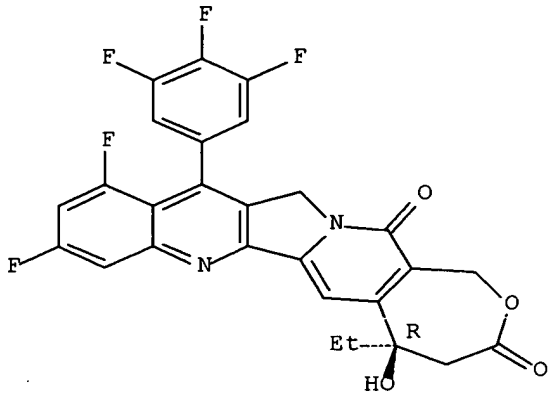
RN 289654-20-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,5-difluorophenyl)-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



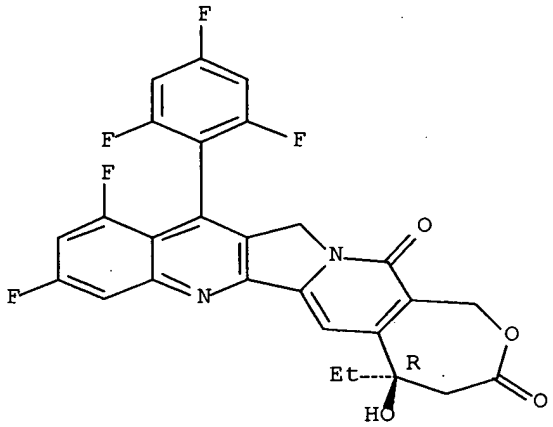
RN 289654-21-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3,4,5-trifluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



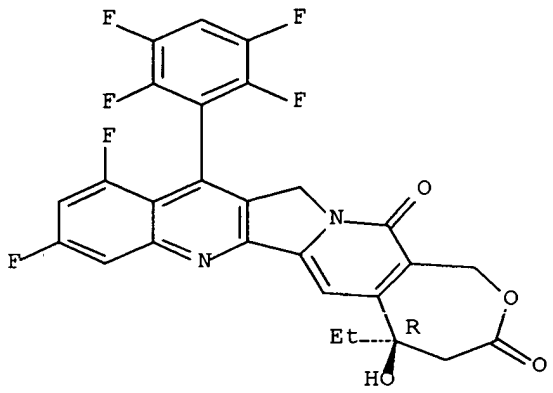
RN 289654-23-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2,4,6-trifluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



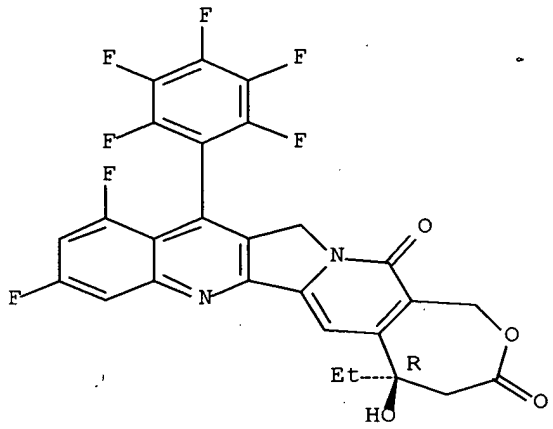
RN 289654-24-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2,3,5,6-tetrafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



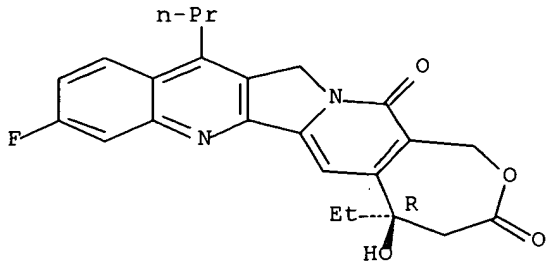
RN 289654-25-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(pentafluorophenyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



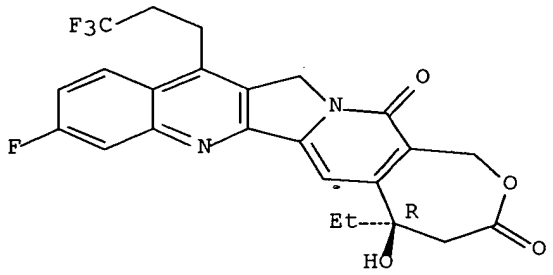
RN 289654-26-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-propyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



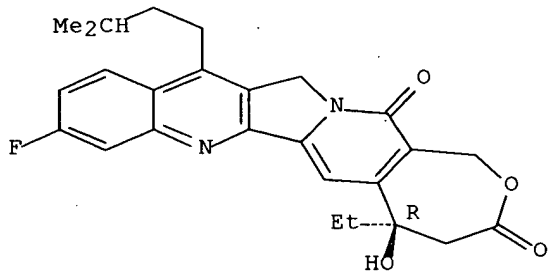
RN 289654-27-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3,3,3-trifluoropropyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



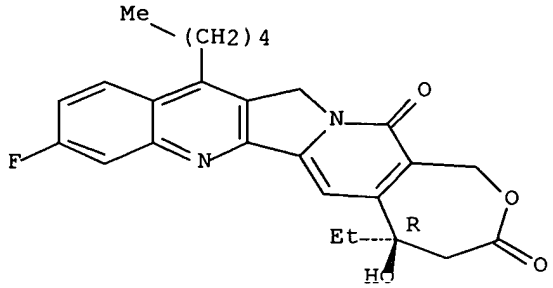
RN 289654-28-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3-methylbutyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



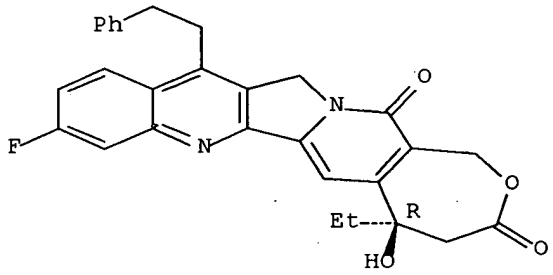
RN 289654-29-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-pentyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



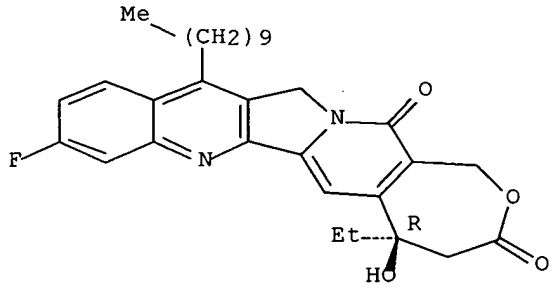
RN 289654-30-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2-phenylethyl)-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 289654-31-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-decyl-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA
INDEX NAME)

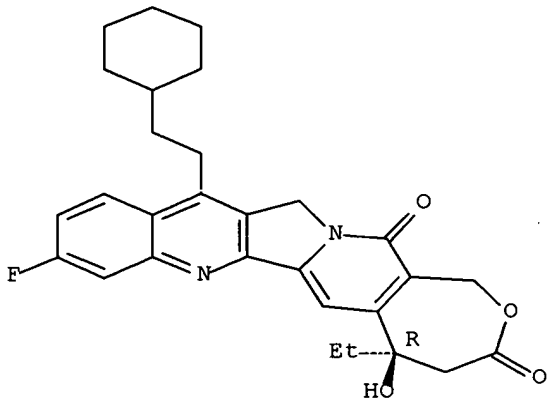
Absolute stereochemistry.



RN 289654-32-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2-cyclohexylethyl)-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-,

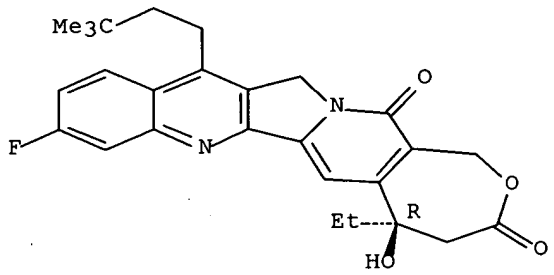
(5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



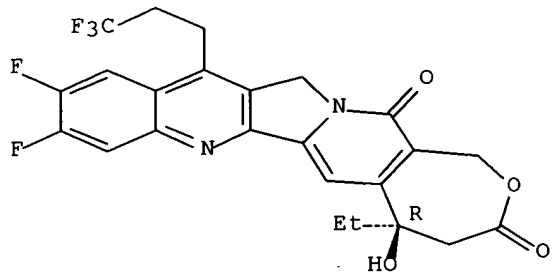
RN 289654-33-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,3-dimethylbutyl)-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



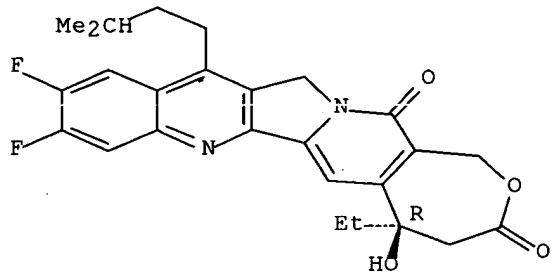
RN 289654-34-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3,3,3-trifluoropropyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



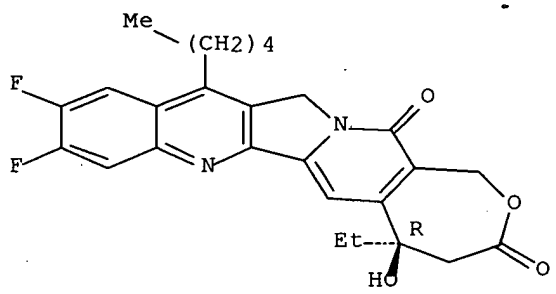
RN 289654-35-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3-methylbutyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



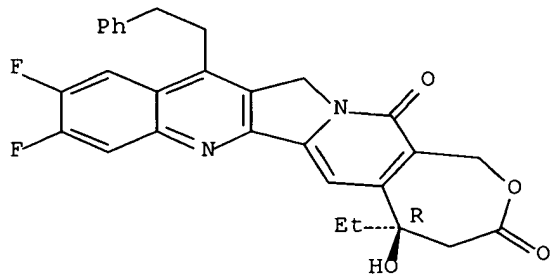
RN 289654-36-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-pentyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



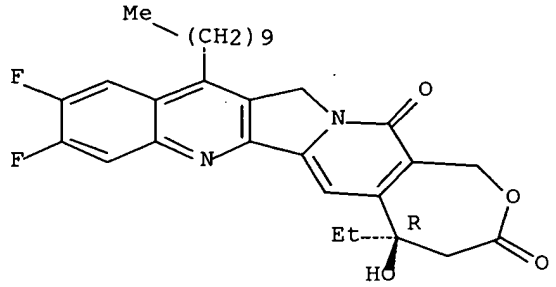
RN 289654-37-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2-phenylethyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



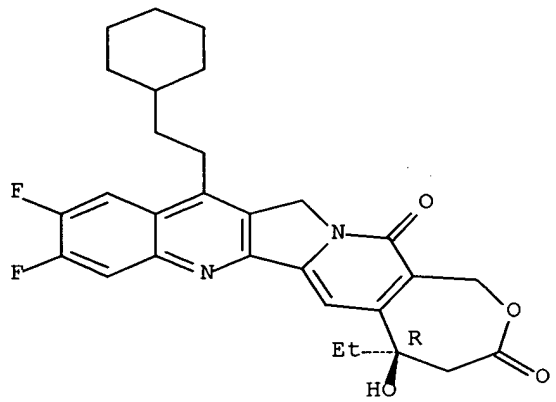
RN 289654-38-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-decyl-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



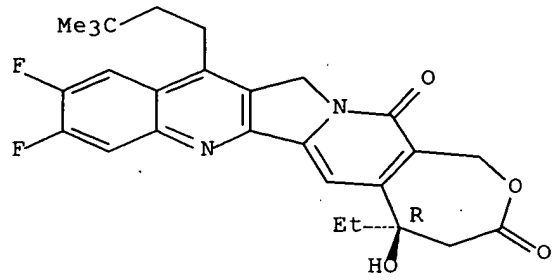
RN 289654-39-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2-cyclohexylethyl)-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-
, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



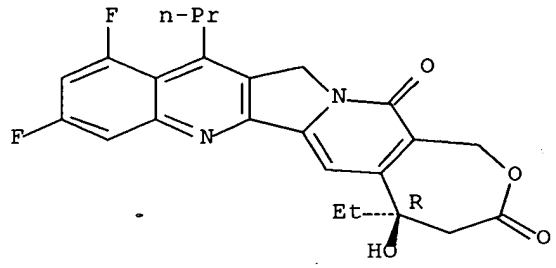
RN 289654-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,3-dimethylbutyl)-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-
, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



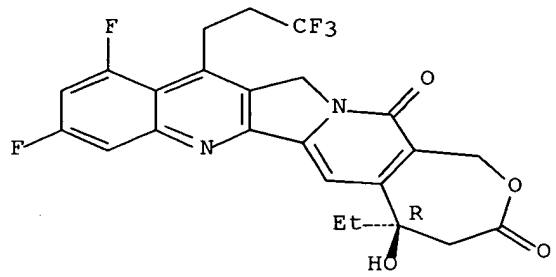
RN 289654-41-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-propyl-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



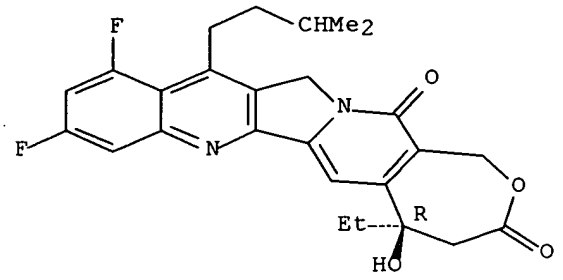
RN 289654-42-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3,3,3-trifluoropropyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



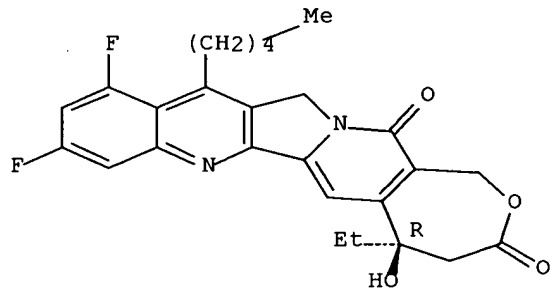
RN 289654-43-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(3-methylbutyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



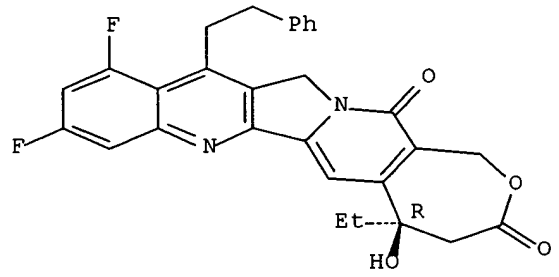
RN 289654-44-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-pentyl-, (5R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



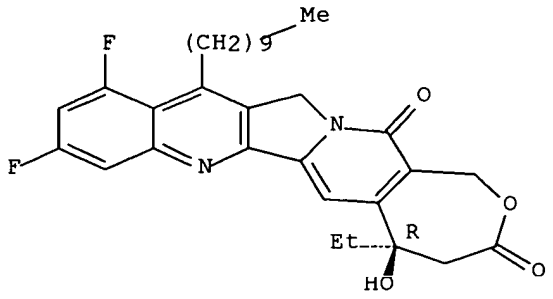
RN 289654-45-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2-phenylethyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



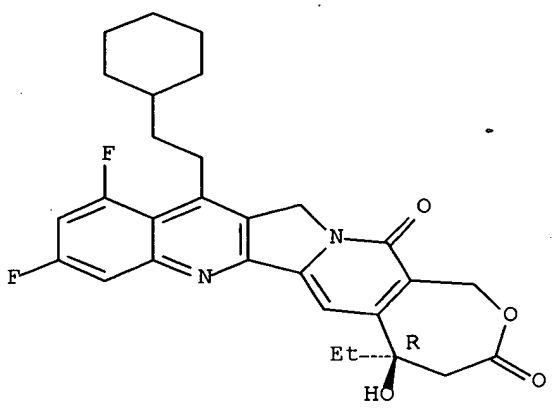
RN 289654-46-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-decyl-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.



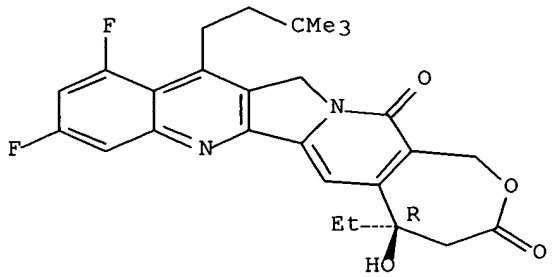
RN 289654-47-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2-cyclohexylethyl)-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



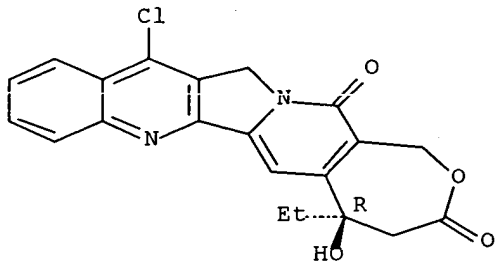
RN 289654-48-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(3,3-dimethylbutyl)-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



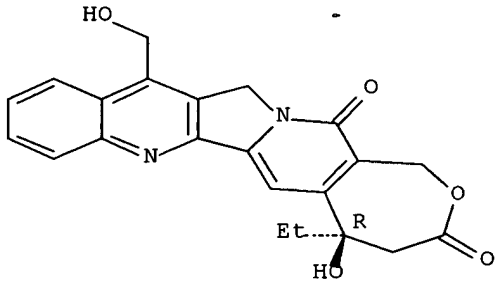
RN 289654-49-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



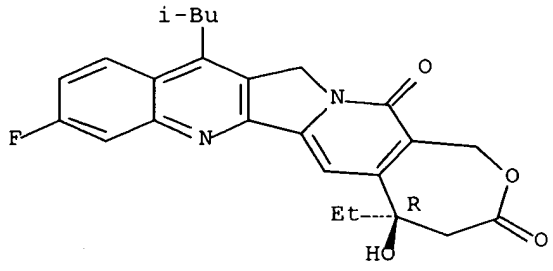
RN 289654-50-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(hydroxymethyl)-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



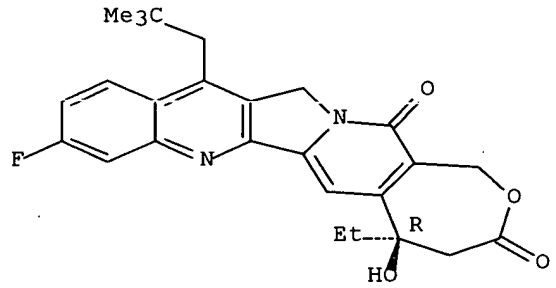
RN 289654-51-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(2-methylpropyl)-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



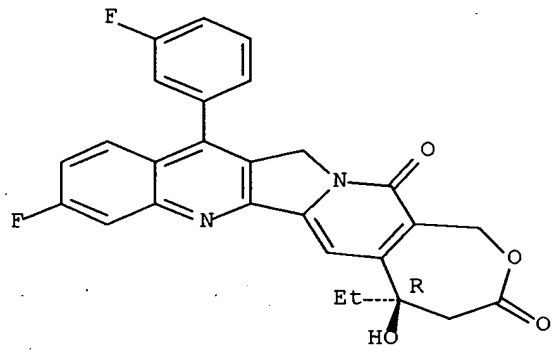
RN 289654-52-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2,2-dimethylpropyl)-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



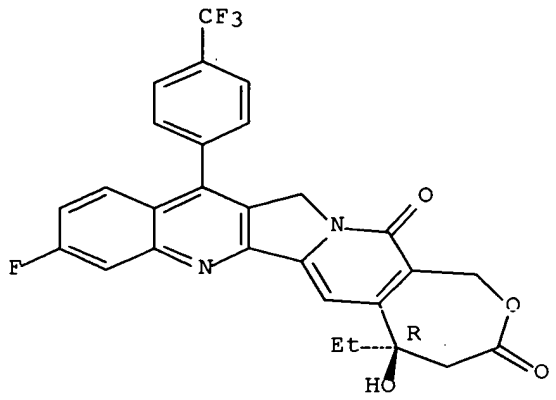
RN 289654-53-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-12-(3-fluorophenyl)-1,4,5,13-tetrahydro-5-hydroxy-, (5R)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



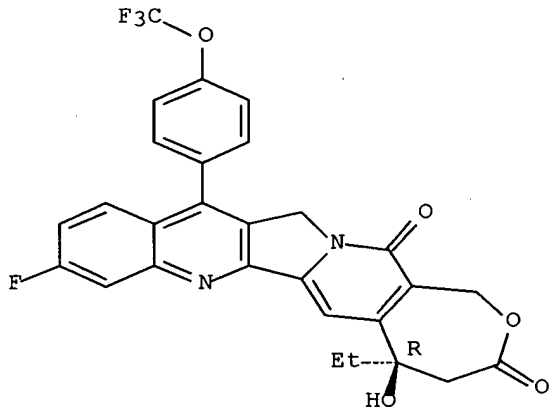
RN 289654-54-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[4-(trifluoromethyl)phenyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



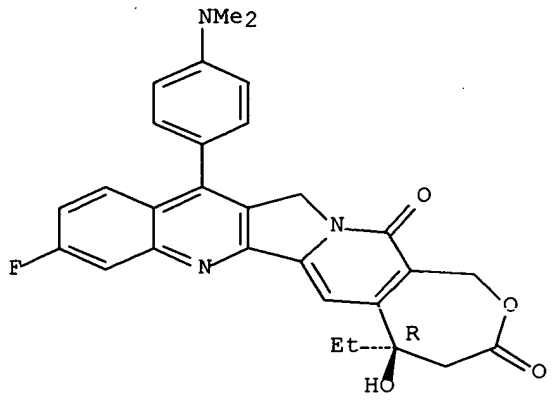
RN 289654-55-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[4-(trifluoromethoxy)phenyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



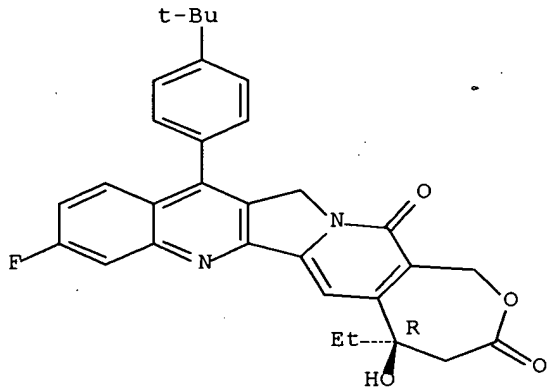
RN 289654-56-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[4-(dimethylamino)phenyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



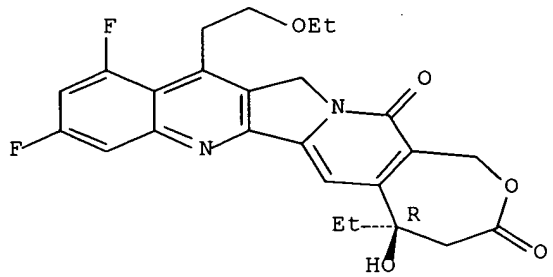
RN 289654-57-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[4-(1,1-dimethylethyl)phenyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



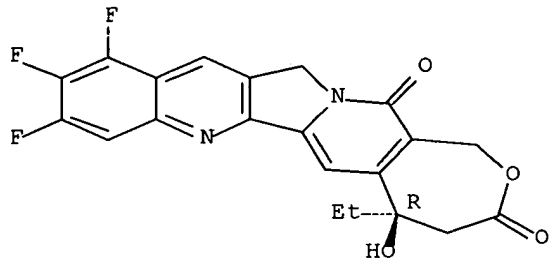
RN 289654-58-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-(2-ethoxyethyl)-5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



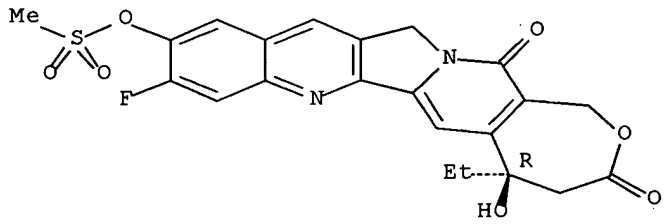
RN 289654-59-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9,10,11-trifluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry.



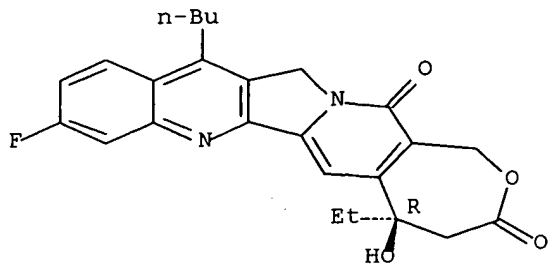
RN 289654-60-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-[(methylsulfonyl)oxy]-
,
(5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



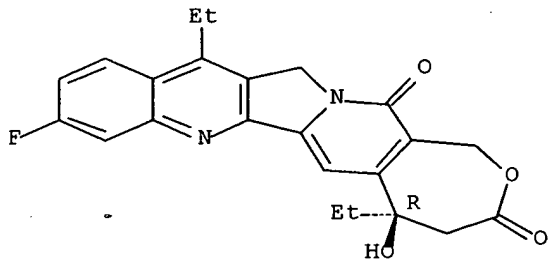
RN 289654-71-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
12-butyl-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI)
(CA
INDEX NAME)

Absolute stereochemistry.



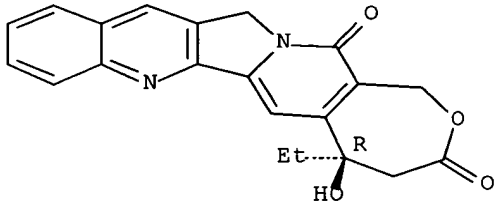
RN 289654-73-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **186669-19-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of optically pure camptothecin analogs for pharmaceutical use as anticancer agents)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

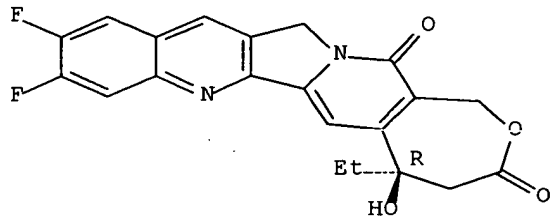
Absolute stereochemistry. Rotation (+).



IT **220997-97-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of optically pure camptothecin analogs for pharmaceutical use as anticancer agents)
RN 220997-97-7 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

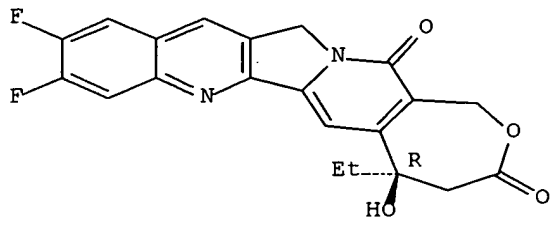
L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2000:587727 CAPLUS
DN 134:36562
TI BN-80915, Beaufour-Ipsen
AU Osheroff, Neil
CS Department of Biochemistry, Vanderbilt University School of Medicine, Nashville, TN, 37232-0146, USA
SO Current Opinion in Oncologic, Endocrine & Metabolic Investigational Drugs (2000), 2(3), 320-323
CODEN: COODF2; ISSN: 1464-8466
PB PharmaPress Ltd.
DT Journal; General Review
LA English
AB A review with 23 refs. Biomeasure and Institut Henri Beaufour, subsidiaries of Beaufour-Ipsen, are developing a series of homocamptothecin topoisomerase I inhibitors, which include BN-80915 and BN-80927, for the potential treatment of cancer. Phase I clin. trials of the lead compd., BN-80915, were initiated in Jan. 1999. Phase II studies are predicted to commence by the end of 2000. In June 2000, it was confirmed that BN-80245, the prototype compd. in this series, is not in (pre)clin. development and is being used as a research tool. BN-80915 was the lead compd. by 1998. BN-80915 is a difluorinated E-ring-modified camptothecin, with a 7-membered .beta.-hydroxylactone ring instead of the 6-membered .alpha.-hydroxylactone of classical camptothecin derivs.; it displays high toxicity toward tumor cell lines, in vivo oral activity in a no. of human tumor xenograft models at low doses and improved plasma stability, compared to other homocamptothecins. BN-80927, another member of the series, disclosed in 1999, inhibits both topoisomerase I and II in DNA relaxation assays. Preclin. studies have shown that the compd. demonstrates activity in HT-29, SW480 and SW620 colorectal cancer models, the N87 gastric cancer model, the small-cell lung cancer NCI-H82 model and the non-small-cell lung cancer A459 and SKMES models, among others. The compd. has been shown to be much more efficient at stimulating DNA cleavage by topoisomerase I than topotecan or SN-38. In vitro studies to investigate the induction of apoptosis in human myelocytic leukemia cells showed that the decrease of the mitochondrial transmembrane potential and the intracellular pH is more pronounced with BN-80915 than with topotecan or camptothecin, which may provide insight into the mechanism of action of the compd.
IT **220997-97-7P**, BN 80915 **220997-99-9P**, BN 80927
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or

effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(antitumor pharmacol. of BN-80915 and BN 80927)

RN 220997-97-7 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

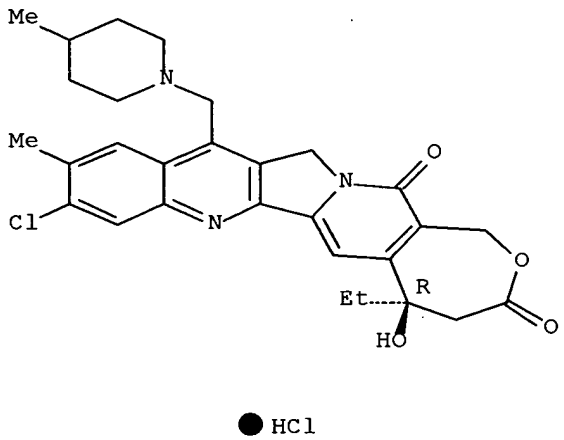
Absolute stereochemistry. Rotation (+).



RN 220997-99-9 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



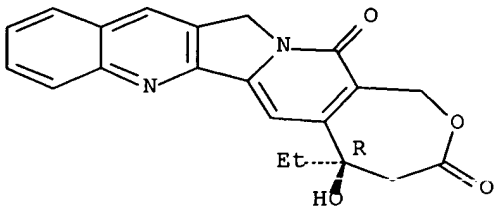
● HCl

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2000:307978 CAPLUS
DN 133:202726
TI Homocamptothecin, an E-ring-modified camptothecin, exerts more potent antiproliferative activity than other topoisomerase I inhibitors in human colon cancers obtained from surgery and maintained in vitro under histotypical culture conditions
AU Philippart, Patrick; Harper, Luke; Chaboteaux, Carole; Decaestecker, Christine; Bronckart, Yves; Gordover, Laurence; Lesueur-Ginot, Laurence; Malonne, Hughes; Lavergne, Olivier; Bigg, Dennis C. H.; Da Costa, Pierre Mendes; Kiss, Robert
CS Departement de Chirurgie, Centre Hospitalier Universitaire Brugmann, Brussels, 1090, Belg.
SO Clinical Cancer Research (2000), 6(4), 1557-1562
CODEN: CCREF4; ISSN: 1078-0432
PB American Association for Cancer Research
DT Journal
LA English
AB Topoisomerase I (Topo I) is overexpressed in cancer colon tissues compared with normal colon tissues. Several anti-Topo I inhibitors are already successfully used in the clinic. We illustrate here the antiproliferative activity of a new class of Topo I inhibitors, i.e., E-ring-modified camptothecins with enhanced lactone stability. Forty-three human colon cancers were obtained from surgical resection and maintained under organotypical culture conditions for 48 h. Cell proliferation was assessed in these ex vivo tumor tissue cultures by tritiated thymidine autoradiog. As a validation of the methodol., we first analyzed in our model the antiproliferative activity of two clin. active topoisomerase II (Topo II) inhibitors, Adriamycin and etoposide, which are not active for colon cancers; and three Topo I inhibitors, camptothecin (CPT) and two clin. active compds. (esp. for colon cancers), i.e., topotecan and the active metabolite of irinothecan, SN-38. We then compared the antiproliferative activity of CPT, topotecan, and SN-38 against those of two investigational E-ring-modified camptothecins, i.e., BN80245 and BN80915. Three concns. (1, 10, and 100 nM) were studied for each compd. The results indicate that the three Topo I inhibitors used as refs., i.e., CPT, irinothecan, and SN-38, were much more active than the two Topo II inhibitors, i.e., Adriamycin and etoposide, with SN-38 being the most efficient. The two investigational compds. BN80245 and BN80915 exerted higher antiproliferative activity than the three anti-Topo I ref. compds., with the highest activity obsd. for BN80915.
IT **186669-19-2 220997-97-7**, BN 80915
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproliferative activity of Topo I inhibitors in human colon cancer)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

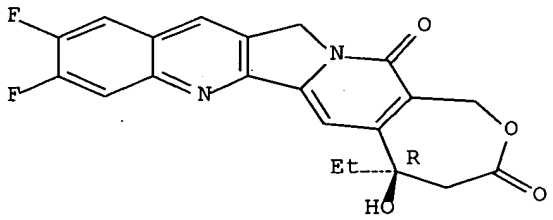
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

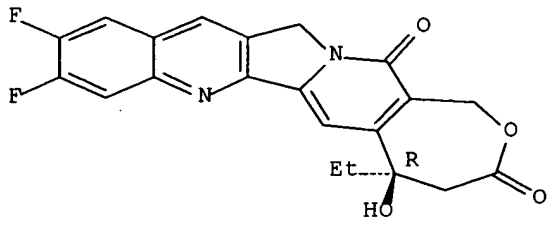
Absolute stereochemistry. Rotation (+).



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

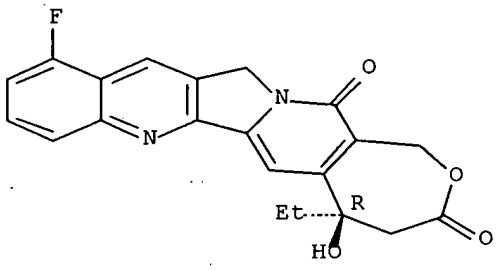
L4 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 2000:301517 CAPLUS
DN 133:114585
TI Topoisomerase I-Mediated Antiproliferative Activity of Enantiomerically Pure Fluorinated Homocamptothecins
AU Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Le Breton, Christine; Manginot, Eric; Cazaux, Jean-Bernard; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO Journal of Medicinal Chemistry (2000), 43(11), 2285-2289
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Homocamptothecin (hCPT) is an E-ring modified camptothecin (CPT) analog bearing a methylene spacer between the alc. and carboxyl functions of the CPT lactone. Combining pronounced inhibitory activity of topoisomerase I (Topo I) with enhanced plasma stability, hCPT constitutes an attractive template for the elaboration of new anticancer agents. Fluorinated hCPT analogs, prepd. in enantiomerically pure form, were assayed by their stimulation of Topo I-mediated DNA cleavage. Translation into cytotoxicity against tumor cells was evaluated on HT29 human colon adenocarcinoma and on the multidrug resistant lung and bladder tumor cell lines, A549 and T24r. Good correlation is obsd. between the ability of the drugs to stimulate Topo I-mediated DNA cleavage and the resp. 50% inhibitory concns. (IC50 values) of the HT29, A549, and T24r cell growth.
Fluorine substitution in the A-ring of hCPT was found to have a pronounced influence on biol. activity, providing several compds. which are .ltoreq.100-fold more potent than CPT in terms of IC50. Among these, 10,11-difluoro-hCPT has been selected for further development.
IT **220997-97-7P 284684-27-1P 284684-28-2P**
284684-29-3P 284684-31-7P 284684-32-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(topoisomerase I-mediated antiproliferative activity against tumor cells of enantiomerically pure fluorinated homocamptothecins in relation to DNA cleavage and pharmacokinetics)
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



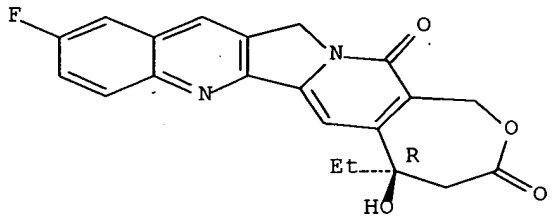
RN 284684-27-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-11-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



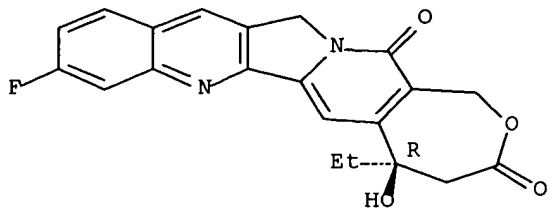
RN 284684-28-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



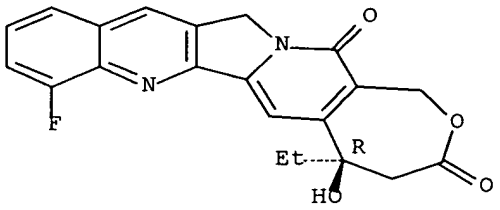
RN 284684-29-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



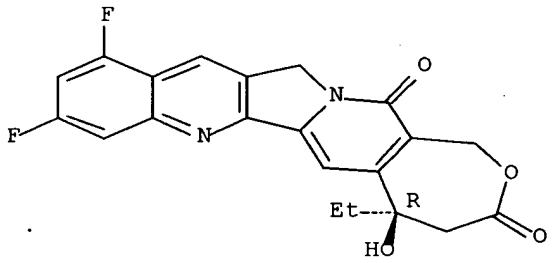
RN 284684-31-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-8-fluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



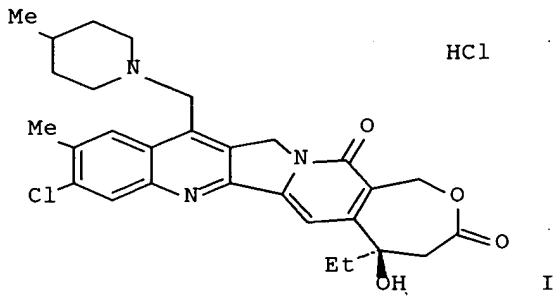
RN 284684-32-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,11-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

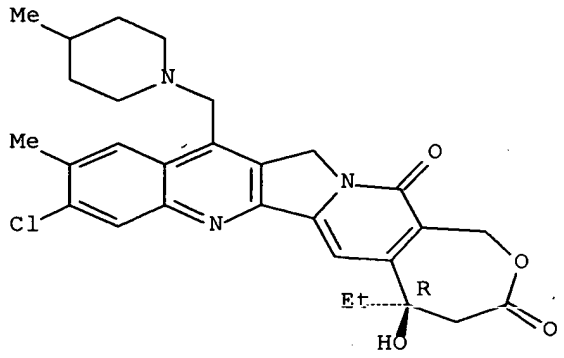
L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1999:614150 CAPLUS
DN 131:351522
TI BN 80927: a novel homocamptothecin with inhibitory activities on both topoisomerase I and topoisomerase II
AU Lavergne, Olivier; Harnett, Jeremiah; Rolland, Alain; Lanco, Christophe; Lesueur-Ginot, Laurence; Demarquay, Daniele; Huchet, Marion; Coulomb, Helene; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(17), 2599-2602
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I

AB BN 80927 (I), a novel homocamptothecin deriv., inhibits both topoisomerase I and topoisomerase II mediated DNA relaxation and shows pronounced cytotoxicity against HT29, SKOV-3, DU145 and MCF7 human tumor cell lines.
IT **220997-99-9P**, BN 80927
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and inhibitory activities of homocamptothecin BN 80927 on both topoisomerase I and II)
RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



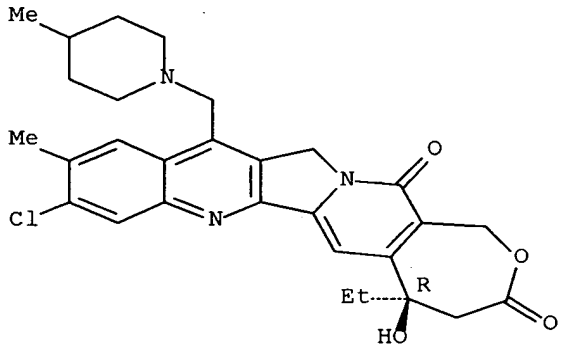
● HCl

IT **220998-10-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(synthesis and inhibitory activities of homocamptothecin BN 80927 on both topoisomerase I and II)

RN 220998-10-7 CAPLUS

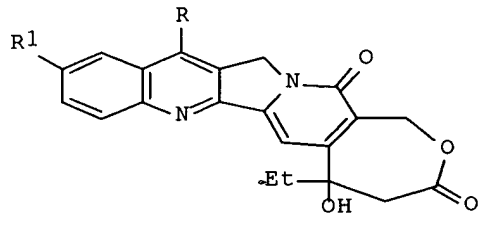
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

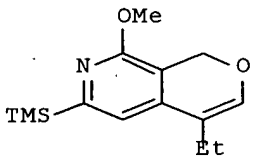


RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1999:455126 CAPLUS
DN 131:299588
TI Novel A,B,E-Ring-Modified Camptothecins Displaying High Lipophilicity and
Markedly Improved Human Blood Stabilities
AU Bom, David; Curran, Dennis P.; Chavan, Ashok J.; Kruszewski, Stefan; Zimmer, Stephen G.; Fraley, Kimberly A.; Burke, Thomas G.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Journal of Medicinal Chemistry (1999), 42(16), 3018-3022
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 131:299588
GI

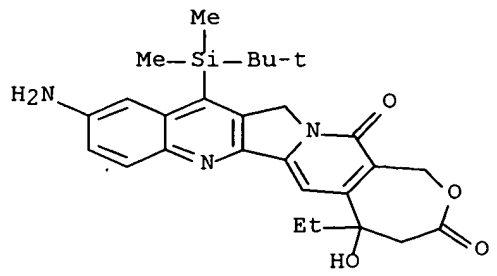


I

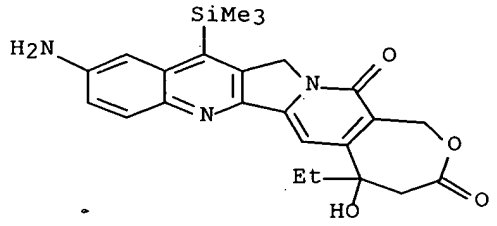


II

AB The camptothecins I (R = Me3CSiMe2, Me3Si; R1 = NH2, OH, H) were prepd. starting from enol ether II. A variety of anal. and biophys. methods were employed to compare the blood component interactions and blood stabilities of I with camptothecin. I are potent topoisomerase I inhibitors that are stable not only in the mouse blood but human blood.
IT **247043-96-5P 247043-97-6P**, DB 38 **247043-98-7P**, DB 91 **247043-99-8P**, DB 81
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(novel A,B,E-ring-modified camptothecins displaying high lipophilicity and markedly improved human blood stabilities)
RN 247043-96-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

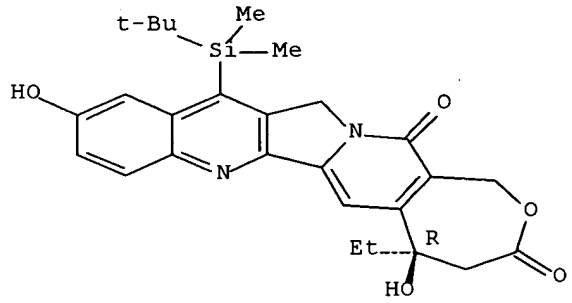


RN 247043-97-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-amino-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(trimethylsilyl)-(9CI)
(CA INDEX NAME)

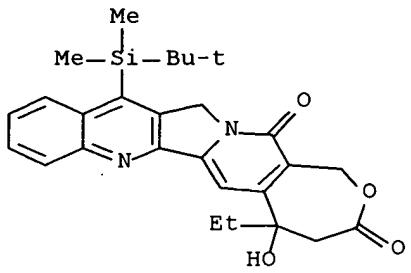


RN 247043-98-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



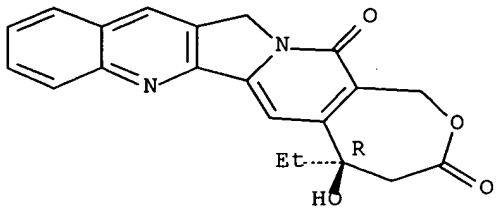
RN 247043-99-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(1,1-dimethylethyl)dimethylsilyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1999:408033 CAPLUS
DN 131:193738
TI Homocamptothecin, an E-ring modified camptothecin with enhanced lactone stability, retains topoisomerase I-targeted activity and antitumor properties
AU Lesueur-Ginot, Laurence; Demarquay, Daniele; Kiss, Robert; Kasprzyk, Philip G.; Dassonneville, Laurent; Bailly, Christian; Camara, Jose; Lavergne, Olivier; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO Cancer Research (1999), 59(12), 2939-2943
CODEN: CNREA8; ISSN: 0008-5472
PB AACR Subscription Office
DT Journal
LA English
AB Homocamptothecin (hCPT) is a semisynthetic analog of camptothecin (CPT) with a seven-membered .beta.-hydroxylactone resulting from the insertion of a methylene spacer between the alc. moiety and the carboxyl function of the naturally occurring six-membered .alpha.-hydroxylactone of CPT. This E-ring modification provides a less reactive lactone with enhanced stability and decreased protein binding in human plasma. Biol. testing against CPT revealed that, instead of being detrimental, the modified lactone of hCPT has a pos. impact on topoisomerase I (Topo I) poisoning properties. In vitro tests showed hCPT to fully conserve the ability to stabilize Topo I-DNA cleavage complexes and to stimulate a higher level of DNA cleavage than CPT. A similar trend toward improvement was also obsd. in antiproliferative assays with human tumor cell lines (including cells overexpressing P-glycoprotein). In two distinct in vivo models, using L1210 murine leukemia or human colon carcinoma HT29, hCPT was found to be more efficacious than CPT. The slow, but irreversible, hydrolysis of hCPT, instead of the fast equil. of CPT, may account for its good in vivo activity. Overall, these results provide evidence that a highly reactive lactone is not a requisite for the Topo I-mediated antitumor activity of CPT analogs, and that hCPT is an interesting pharmacol. tool with improved soln. behavior as well as a promising new template for the prepn. of more efficacious Topo I poisons.
IT **186669-19-2**, E-Homocamptothecine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(homocamptothecin, E-ring modified camptothecin with enhanced lactone stability, retains topoisomerase I-targeted activity and antitumor properties)
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1999:184257 CAPLUS
DN 130:223476
TI Preparation of optically pure camptothecin analogs and their intermediates
IN Cazaux, Jean-Bernard; Lavergne, Olivier; Le Breton, Christine; Manginot, Eric; Bigg, Dennis
PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9911646	A1	19990311	WO 1998-FR1768	19980807
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2768431	A1	19990319	FR 1997-10785	19970829
	FR 2768431	B1	20000324		
	CA 2301739	AA	19990311	CA 1998-2301739	19980807
	AU 9889896	A1	19990322	AU 1998-89896	19980807
	EP 1007527	A1	20000614	EP 1998-941567	19980807
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	BR 9811405	A	20000829	BR 1998-11405	19980807
	JP 2001514261	T2	20010911	JP 2000-508685	19980807
	NZ 502862	A	20021025	NZ 1998-502862	19980807
	ZA 9807445	A	19990217	ZA 1998-7445	19980818
	TW 419479	B	20010121	TW 1998-87113646	19980819
	US 6339091	B1	20020115	US 1999-332520	19990614
	NO 2000000995	A	20000228	NO 2000-995	20000228
	US 2002160994	A1	20021031	US 2002-61049	20020130
	US 2003004150	A1	20030102	US 2002-71046	20020206
PRAI	FR 1997-10785	A	19970829		
	GB 1995-12670	A	19950621		
	WO 1996-FR980	W	19960621		
	FR 1996-15774	A	19961220		
	FR 1996-15775	A	19961220		
	FR 1996-15945	A	19961224		
	US 1997-973561	A2	19971202		
	WO 1997-FR2217	W	19971205		
	WO 1997-FR2218	W	19971205		
	WO 1998-FR1768	W	19980807		
	FR 1999-2398	A	19990226		
	US 1999-332520	A3	19990614		
	WO 2000-FR461	W	20000224		
	US 2000-612382	A3	20000707		
	US 2001-806952	W	20010405		

OS MARPAT 130:223476

GI

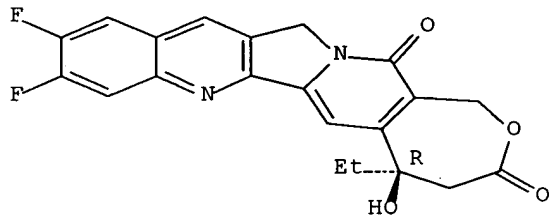
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The camptothecin analogs (+)-5-ethyl-9,10-difluoro-5-hydroxy-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione (I) and (+)-1-[9-chloro-5-ethyl-5-hydroxy-10-methyl-3,15-dioxo-4,5,13,15-tetrahydro-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinoline-12-ylmethyl]-4-methylhexahydropyridinium chloride (II) were prepd. as antitumoral, antiviral or antiparasitic medicines. The invention also concerns a novel synthesis of intermediates of the products. Thus, (+)-5-ethyl-5-hydroxy-1,3,4,5,8,9-hexahydrooxepino[3,4-c]pyridin-3,9-dione (III), prepd. in three steps form tert-Bu 3-(3-benzyloxymethyl-2-methoxy-4-pyridyl)-3-hydroxypentanoate, was treated with 2-chloro-6,7-difluoro-3-quinolinylmethanol followed by cyclization to give I. I inhibited 50% proliferation of SW620 cells at 5.10-9 M.

IT **220997-97-7P 220997-99-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of optically pure camptothecin analogs)

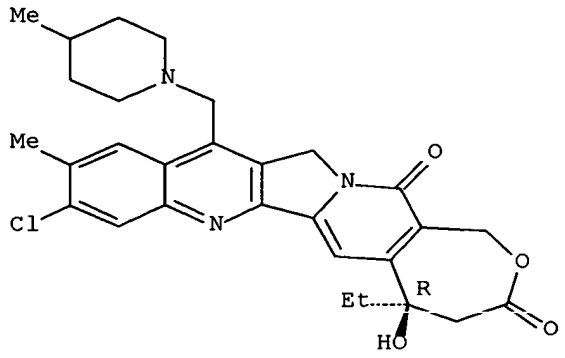
RN 220997-97-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 220997-99-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, monohydrochloride, (5R)- (9CI) (CA INDEX NAME)

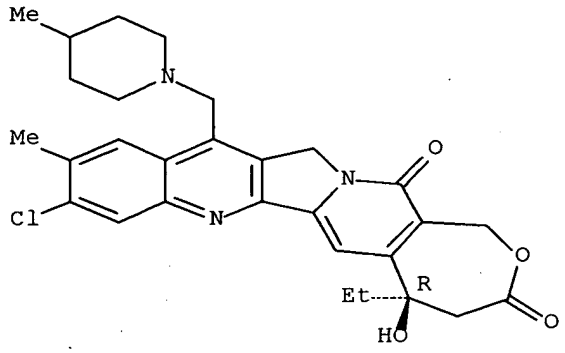
Absolute stereochemistry. Rotation (+).



● HCl

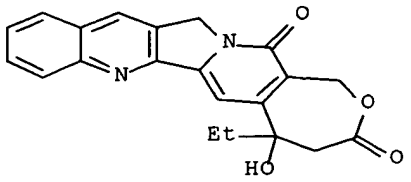
IT **220998-10-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of optically pure camptothecin analogs)
RN 220998-10-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

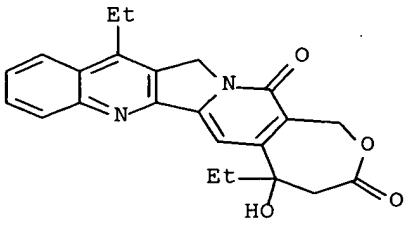


RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

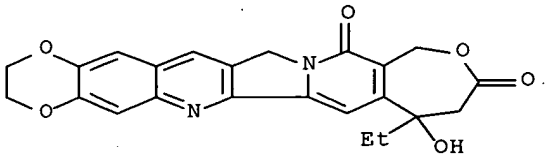
L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1998:772004 CAPLUS
DN 130:125250
TI Homocamptothecins: Synthesis and Antitumor Activity of Novel E-Ring-Modified Camptothecin Analogs
AU Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; Demarquay, Daniele; Prevost, Gregoire; Ulibarri, Gerard; Rolland, Alain; Schiano-Liberatore, Anne-Marie; Harnett, Jeremiah; Pons, Dominique; Camara, Jose; Bigg, Dennis C. H.
CS Institut Henri Beaufour, Les Ulis, F-91966, Fr.
SO Journal of Medicinal Chemistry (1998), 41(27), 5410-5419
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB Homocamptothecin (hCPT), a camptothecin (CPT) analog with a seven membered .beta.-hydroxylactone which combines enhanced plasma stability and potent topoisomerase I (Topo I)-mediated activity, is an attractive template for the elaboration of new anticancer agents. Like CPT, hCPT carries an asym. tertiary alc. and displays stereoselective inhibition of Topo I. The prepn. and biol. screening of racemic hCPT analogs are described. The 10 hCPTs tested were better Topo I inhibitors than CPT. Fluorinated hCPTs were found to have potent cytotoxic activity on A427 and PC-3 tumor cell lines. Their cytotoxicity remained high on the K562adr and MCF7mdr cell lines, which overexpress a functionally active P-glycoprotein. Fluorinated hCPTs were more efficacious in vivo than CPT on HT-29 xenografts. In this model, a tumor growth delay of 25 days was reached with 9,10-difluoro-hCPT at a daily dose of 0.32 mg/kg, compared to 4 days with CPT at 0.625 mg/kg. Thus difluorinated hCPT warrants further investigation as a novel Topo I inhibitor with high cytotoxicity toward tumor cells and promising in vivo efficacy.
IT **186668-40-6P 186668-44-0P 186668-59-7P**
186668-68-8P 186668-69-9P 186668-70-2P
186668-71-3P 186668-75-7P 186668-77-9P
186668-79-1P 186669-19-2P 186669-20-5P
209909-06-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and antitumor activity of homocamptothecin analogs)
RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



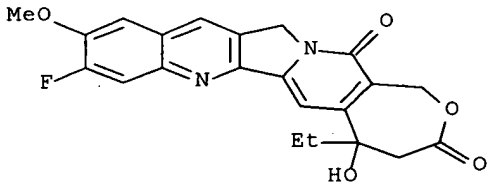
RN 186668-44-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-59-7 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)

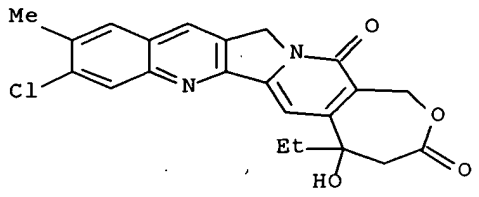


RN 186668-68-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)

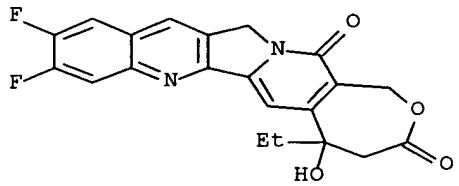


RN 186668-69-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX

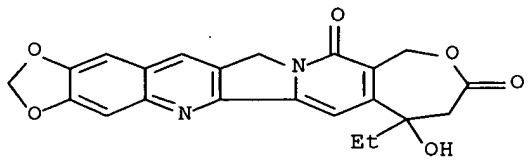
NAME)



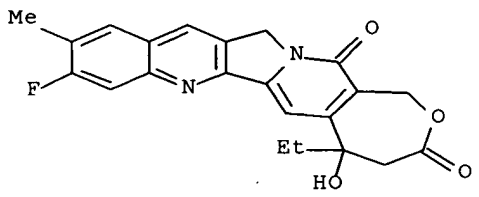
RN 186668-70-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-71-3 CAPLUS
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-
dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)

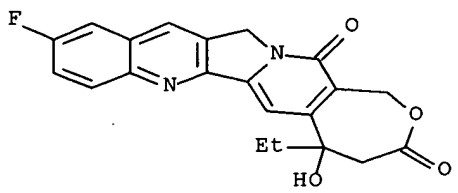


RN 186668-75-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX
NAME)

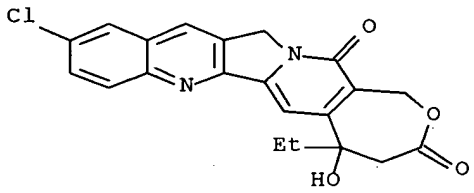


RN 186668-77-9 CAPLUS

CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

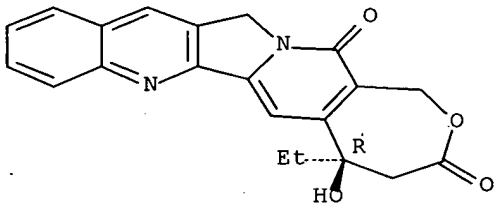


RN 186668-79-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



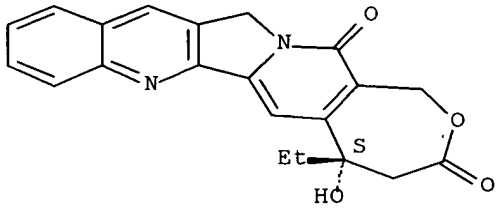
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

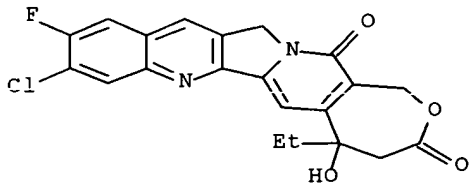


RN 186669-20-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 209909-06-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1998:550712 CAPLUS
DN 129:136346
TI Preparation of camptothecin analogs as antitumors, antivirals, and parasiticides
IN Bigg, Dennis; Lavergne, Olivier; Pla Rodas, Francesc; Pommier, Jacques; Ulibarri, Gerard
PA Societe de Conseils de Recherches et d'Applications Scientifiques SCRAS S.
A, Fr.
SO Fr. Demande, 88 pp.
CODEN: FRXXBL
DT Patent
LA French
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2757514	A1	19980626	FR 1996-15774	19961220
	FR 2757514	B1	19990212		
	WO 9828305	A1	19980702	WO 1997-FR2218	19971205
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	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9853265	A1	19980717	AU 1998-53265	19971205
	AU 734485	B2	20010614		
	EP 946567	A1	19991006	EP 1997-950236	19971205
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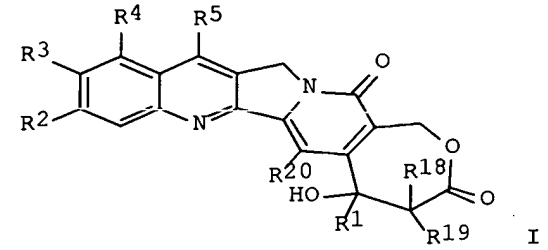
	BR 9714170	A	20000229	BR 1997-14170	19971205
	NZ 335939	A	20000428	NZ 1997-335939	19971205
	JP 2001505922	T2	20010508	JP 1998-528448	19971205
	RU 2194051	C2	20021210	RU 1999-115829	19971205
	ZA 9711129	A	19990503	ZA 1997-11129	19971210
	US 6339091	B1	20020115	US 1999-332520	19990614
	NO 9902998	A	19990818	NO 1999-2998	19990618
	US 2002160994	A1	20021031	US 2002-61049	20020130
	US 2003004150	A1	20030102	US 2002-71046	20020206
PRAI	GB 1995-12670	A	19950621		
	WO 1996-FR980	W	19960621		
	FR 1996-15774	A	19961220		
	FR 1996-15775	A	19961220		
	FR 1996-15945	A	19961224		
	FR 1997-10785	A	19970829		
	US 1997-973561	A2	19971202		
	WO 1997-FR2217	W	19971205		
	WO 1997-FR2218	W	19971205		
	WO 1998-FR1768	W	19980807		
	FR 1999-2398	A	19990226		
	US 1999-332520	A3	19990614		
	WO 2000-FR461	W	20000224		
	US 2000-612382	A3	20000707		
	US 2001-806952	W	20010405		

OS MARPAT 129:136346
GI



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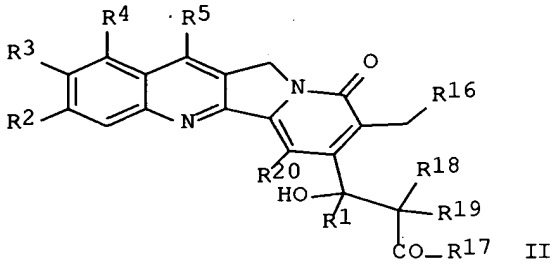
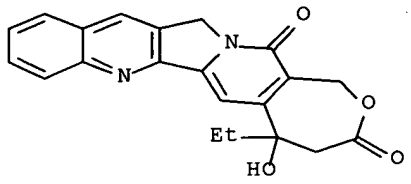


II

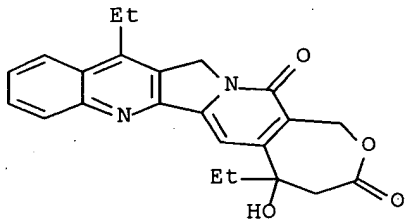
AB Title compds. I and II [R1 = alkyl, alkenyl, alkynyl, etc.; R2, R3, R4 = H, halo, haloalkyl, alkyl, alkenyl, cyano, etc.; R5 = H, halo, haloalkyl, alkyl, alkoxy, alkoxyalkyl, etc.; R16 = H, OH, acyloxy; R17 = OR6, NR6R7; R6, R7 = H, alkyl, hydroxyalkyl, alkylaminoalkyl, etc.; R18, R19 = H, halo, alkyl, alkoxy, OH; R20 = H, halo] are prepd. Thus, 8-formyloxymethyl-7-propionylindolizino[1,2-b]quinolin-9(11)-one, obtained in 2 steps via NaBH4 redn. of (S)-(+)-camptothecin and subsequent oxidative ring cleavage, reacted with tert-Bu bromoacetate in Et2O and THF contg. Zn and chlorotrimethylsilane to give the title compd. tert-Bu .beta.-ethyl-.beta.-hydroxy-.gamma.-(8-hydroxymethyl-9-oxo-11H-indolizino[1,2-b]quinolin-7-yl)propionate. In an in vitro study, 5-ethyl-4,5-dihydro-5-hydroxy-1H-oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15(4H,13H)-dione (also prepd.) at 10 .mu.M effected ca. 58% redn. in the proliferation of L1210.

IT **186668-40-6P 186668-44-0P 186668-63-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of camptothecin analogs as antitumors, antivirals, and parasiticides)

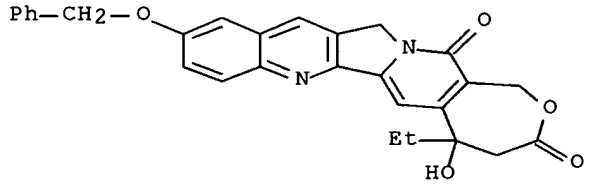
RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-44-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-63-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)



IT **186668-59-7P 186668-65-5P 186668-67-7P**
186668-68-8P 186668-69-9P 186668-70-2P
186668-71-3P 186668-72-4P 186668-73-5P
186668-74-6P 186668-75-7P 186668-77-9P
186668-79-1P 186668-90-6P 186668-94-0P
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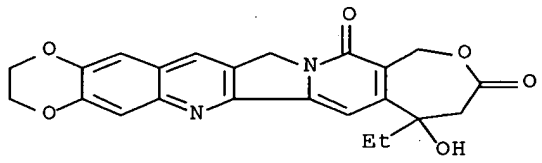
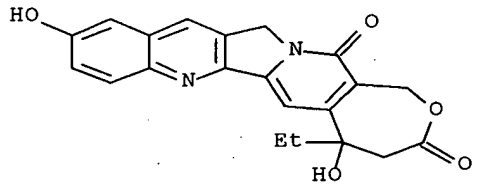
210563-51-2P 210563-53-4P 210563-55-6P
210563-57-8P 210563-60-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as antitumors, antivirals, and parasiticides)

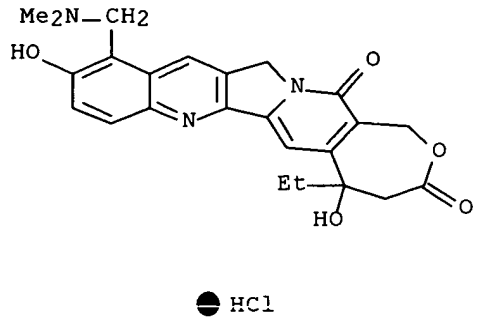
RN 186668-59-7 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)



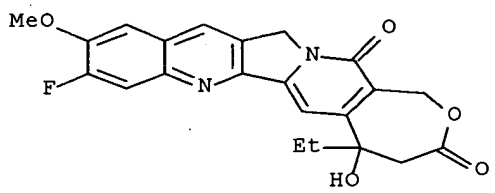
RN 186668-65-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



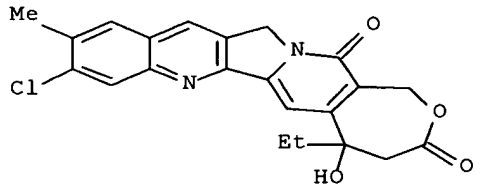
RN 186668-67-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, monohydrochloride (9CI) (CA INDEX NAME)



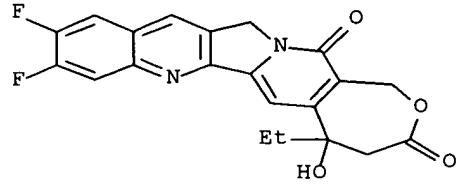
RN 186668-68-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



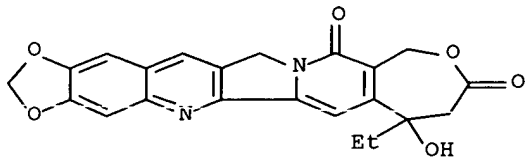
RN 186668-69-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



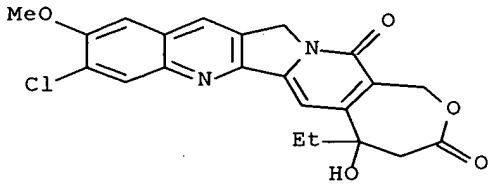
RN 186668-70-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



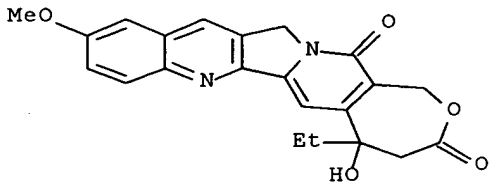
RN 186668-71-3 CAPLUS
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-
dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)



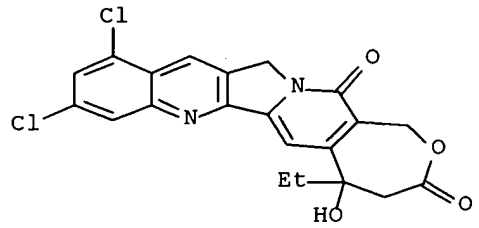
RN 186668-72-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



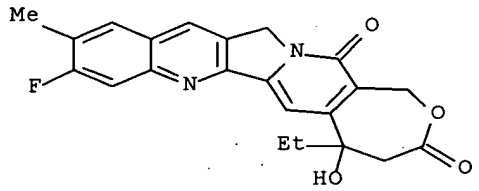
RN 186668-73-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



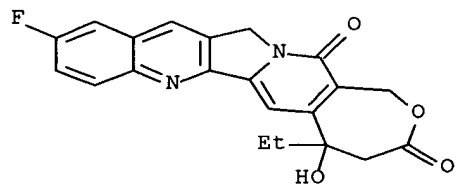
RN 186668-74-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9,11-dichloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



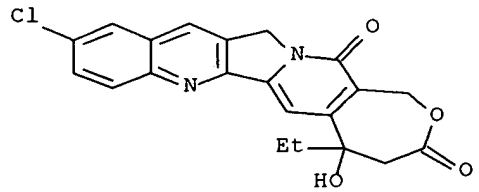
RN 186668-75-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



RN 186668-77-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

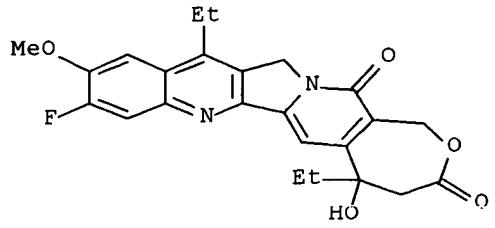


RN 186668-79-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)

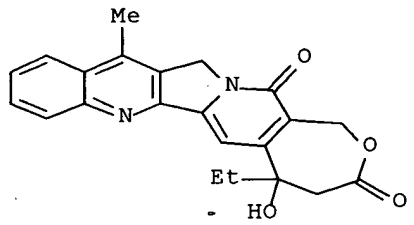


RN 186668-90-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA

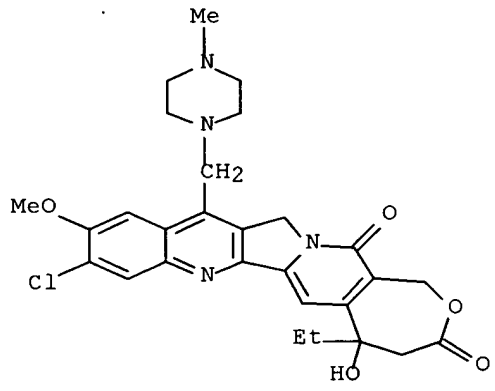
INDEX NAME)



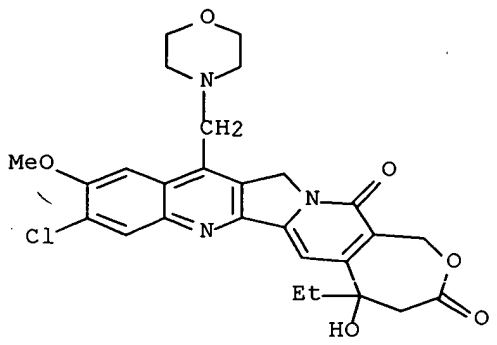
RN 186668-94-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-methyl- (9CI) (CA INDEX NAME)



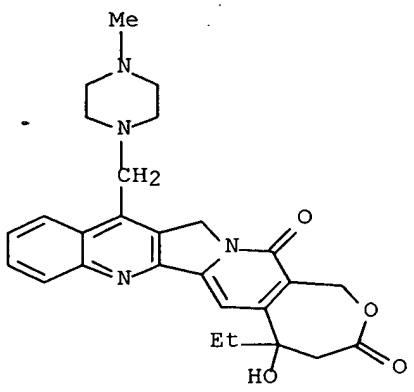
RN 186669-03-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



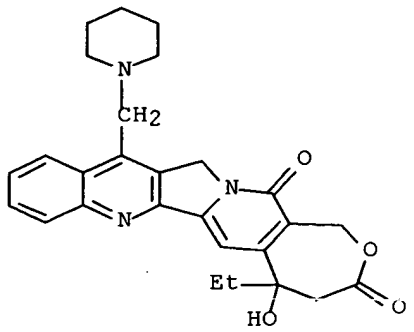
RN 186669-04-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



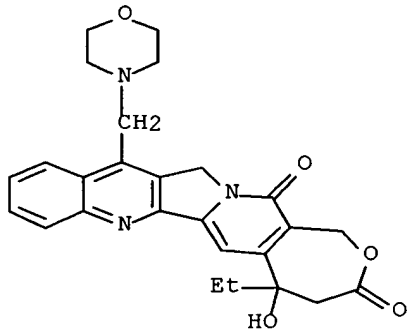
RN 186669-06-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



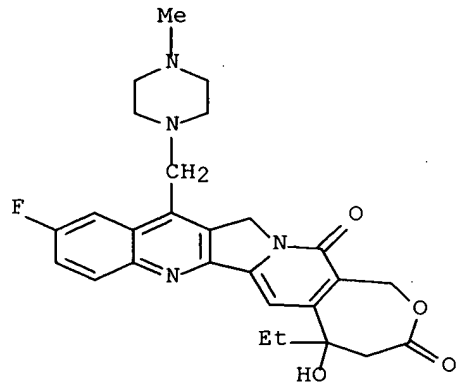
RN 186669-07-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



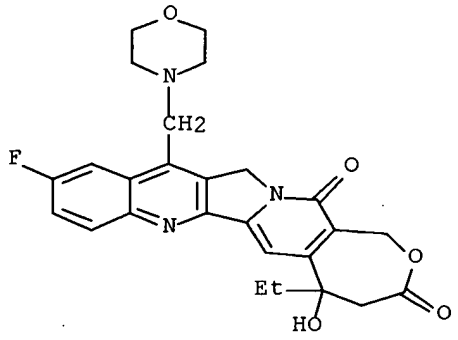
RN 186669-08-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



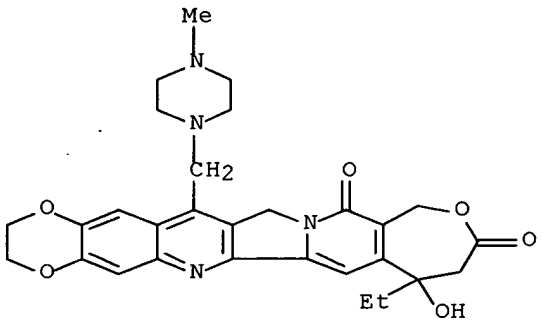
RN 186669-09-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



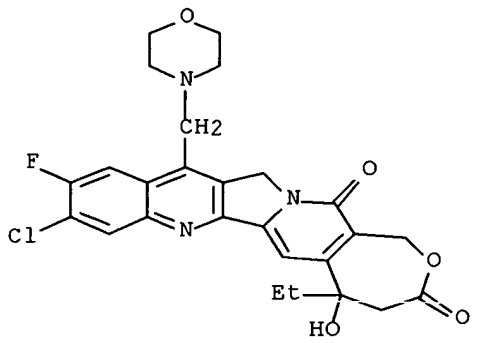
RN 186669-10-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



RN 186669-16-9 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy-16-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

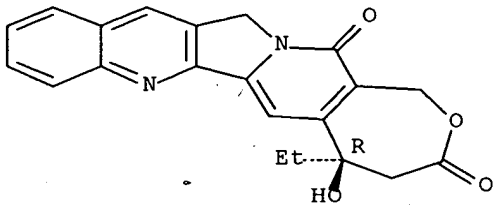


RN 186669-18-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



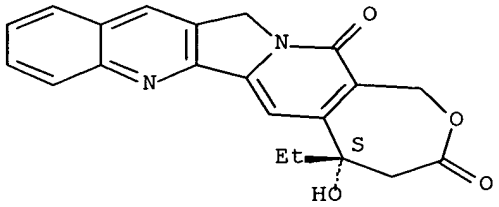
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

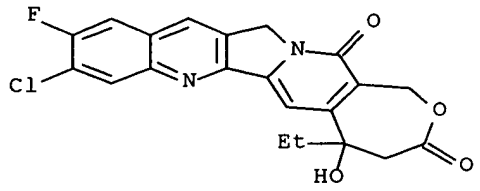


RN 186669-20-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5S)- (9CI) (CA INDEX NAME)

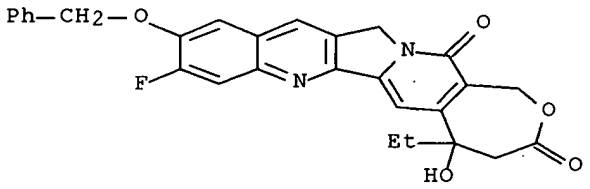
Absolute stereochemistry.



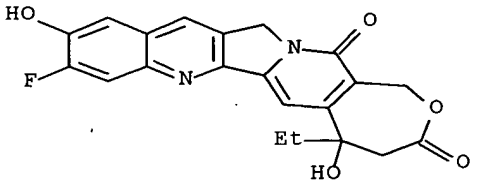
RN 209909-06-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



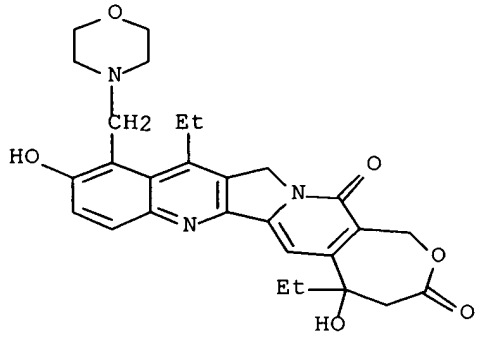
RN 209909-08-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)



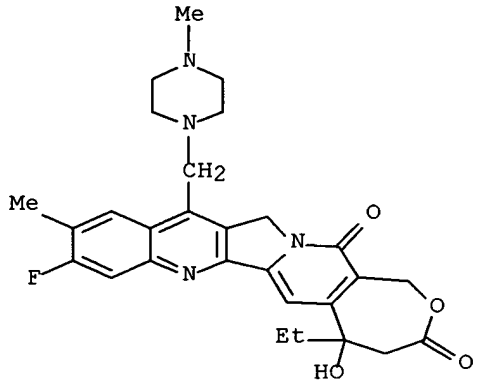
RN 209909-09-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



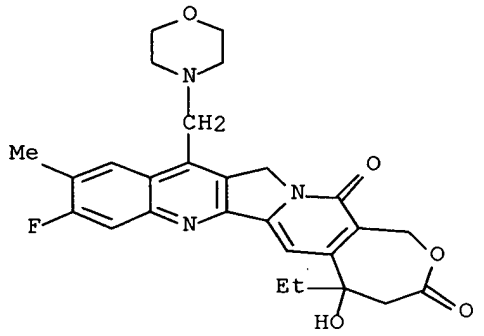
RN 210562-90-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-11-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



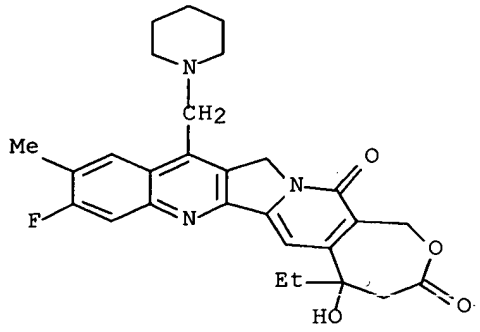
RN 210563-02-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



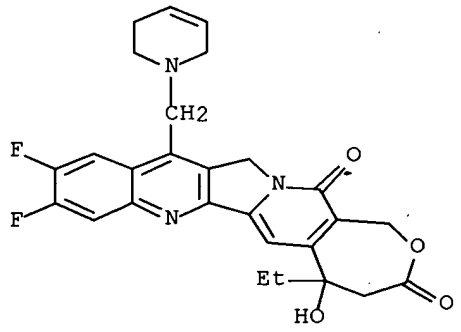
RN 210563-04-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



RN 210563-06-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)

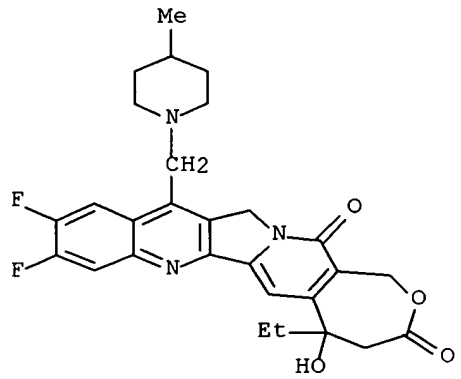


RN 210563-07-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(3,6-dihydro-1(2H)-pyridinyl)methyl]-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

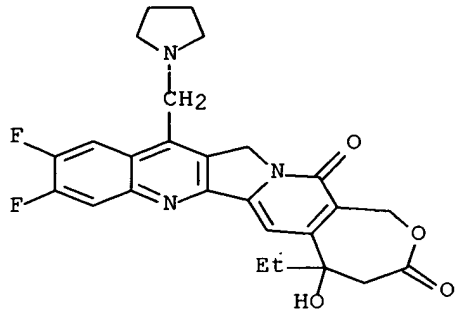


● HCl

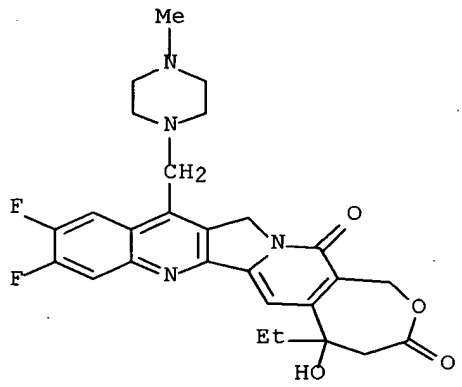
RN 210563-08-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



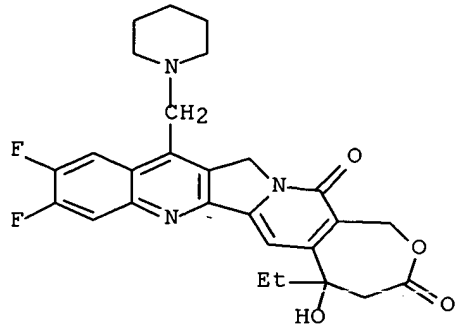
RN 210563-09-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)



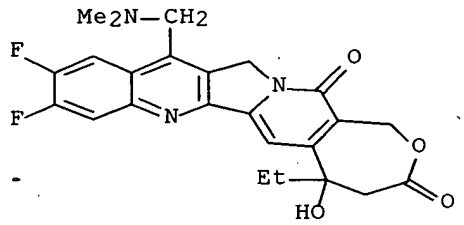
RN 210563-11-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



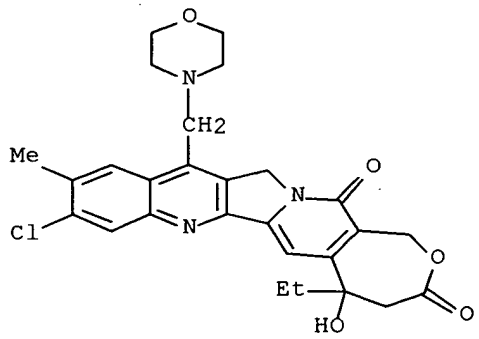
RN 210563-12-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



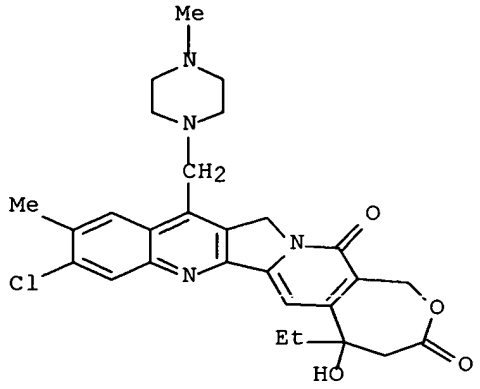
RN 210563-14-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(dimethylamino)methyl]-5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



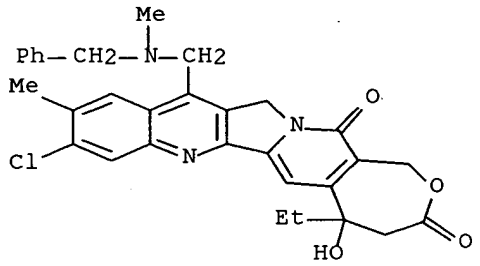
RN 210563-16-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



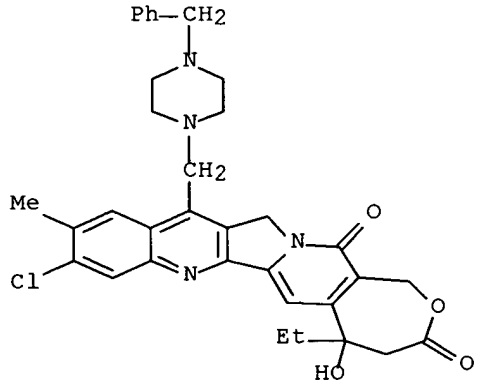
RN 210563-18-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



RN 210563-20-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[[methyl(phenylmethyl)amino]methyl]- (9CI) (CA INDEX NAME)

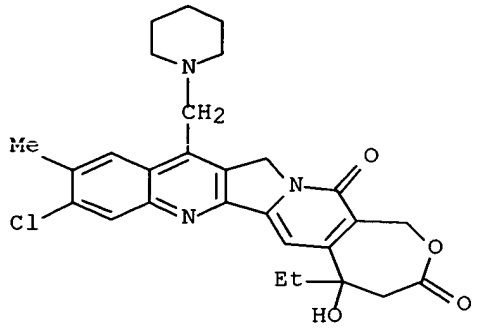


RN 210563-22-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)

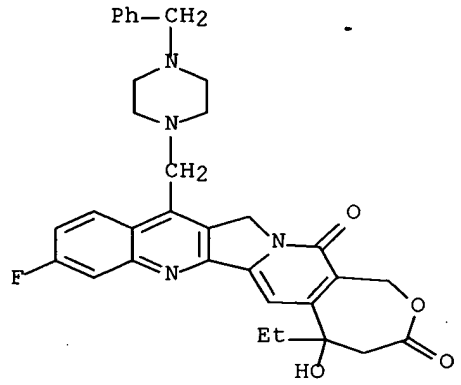


RN 210563-24-9 CAPLUS

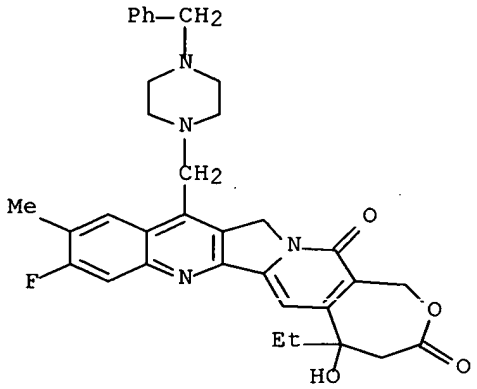
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



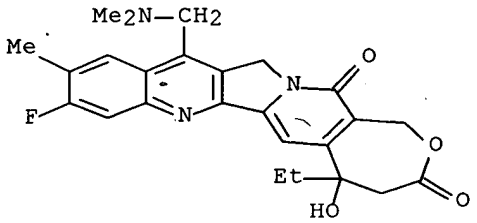
RN 210563-26-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



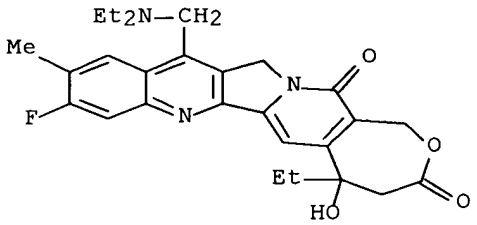
RN 210563-28-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[[4-(phenylmethyl)-1-piperazinyl]methyl]- (9CI) (CA INDEX NAME)



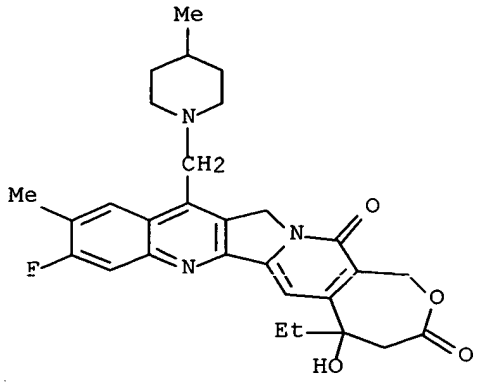
RN 210563-30-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
12-[(dimethylamino)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-
10-methyl- (9CI) (CA INDEX NAME)



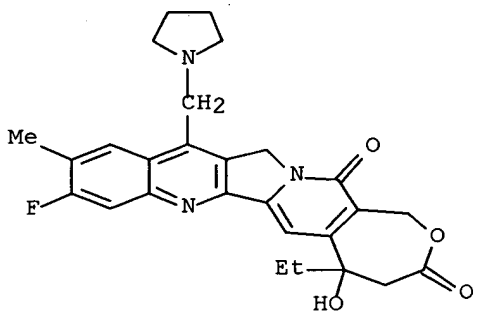
RN 210563-32-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
12-[(diethylamino)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-
10-methyl- (9CI) (CA INDEX NAME)



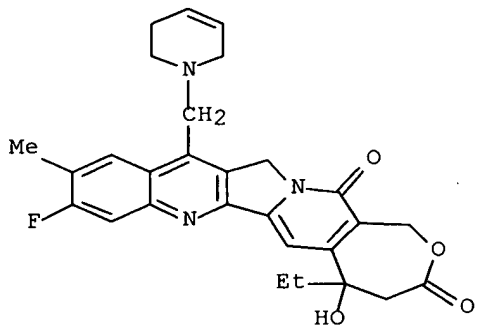
RN 210563-34-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-
piperidinyl)methyl]- (9CI) (CA INDEX NAME)



RN 210563-35-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-(1-pyrrolidinylmethyl)- (9CI) (CA INDEX NAME)

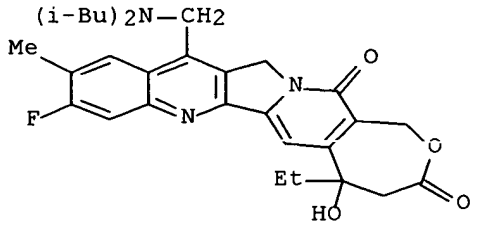


RN 210563-37-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(3,6-dihydro-1(2H)-pyridinyl)methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)

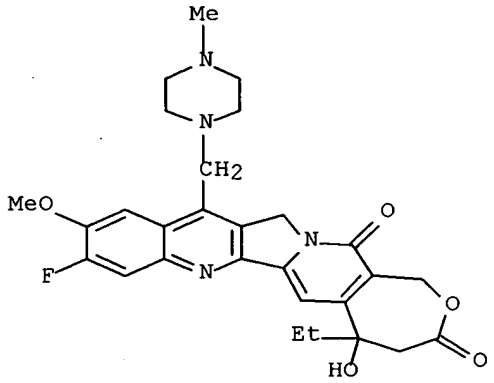


RN 210563-39-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

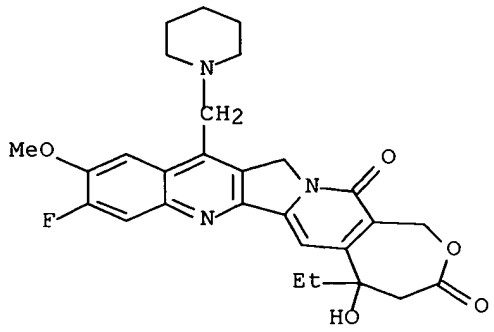
12-[[bis(2-methylpropyl)amino]methyl]-5-ethyl-9-fluoro-1,4,5,13-tetrahydro-
5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



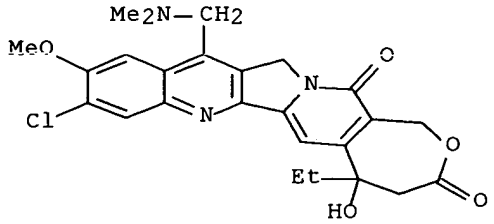
RN 210563-41-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-
piperazinyl)methyl]- (9CI) (CA INDEX NAME)



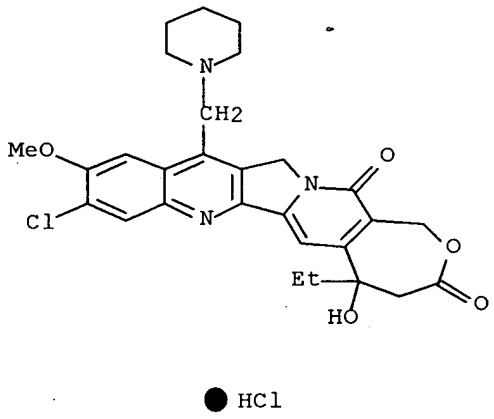
RN 210563-43-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-
piperidinylmethyl)- (9CI) (CA INDEX NAME)



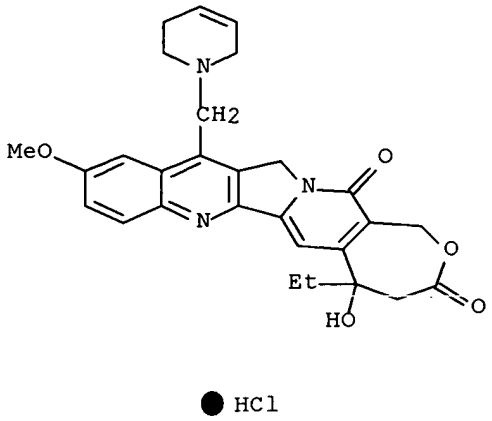
RN 210563-45-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-12-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



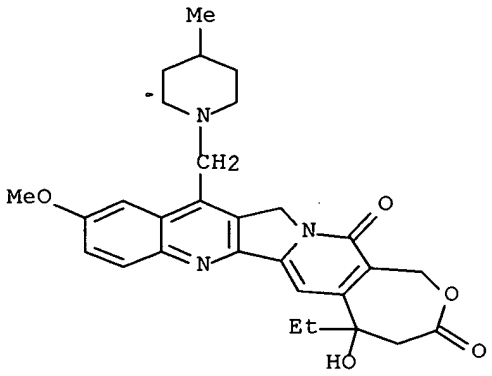
RN 210563-47-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-piperidinylmethyl)-, monohydrochloride (9CI) (CA INDEX NAME)



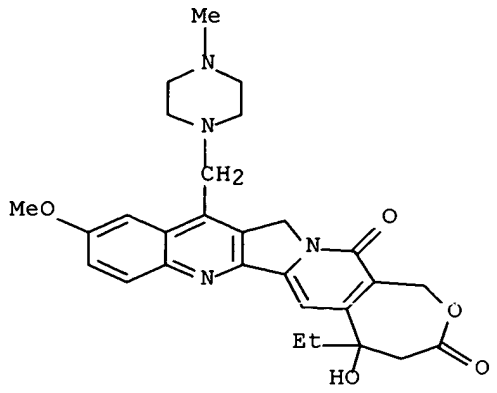
RN 210563-49-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 12-[(3,6-dihydro-1(2H)-pyridinyl)methyl]-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-, monohydrochloride (9CI) (CA INDEX NAME)



RN 210563-51-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



RN 210563-53-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



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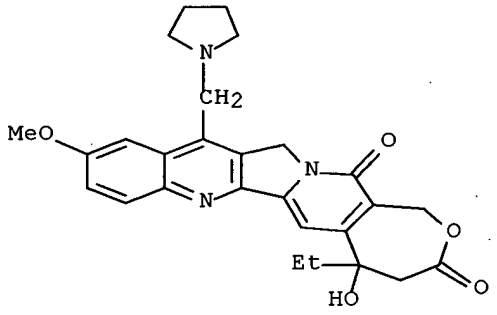
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(1-pyrrolidinylmethyl)-
(9CI) (CA INDEX NAME)



RN 210563-57-8 CAPLUS
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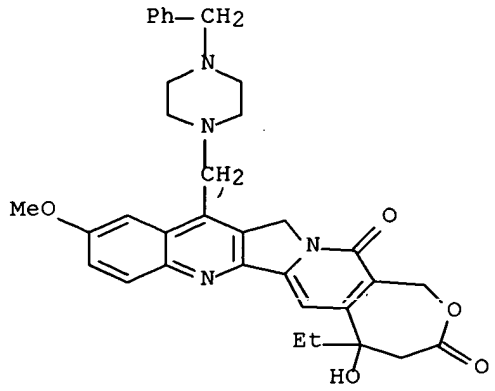
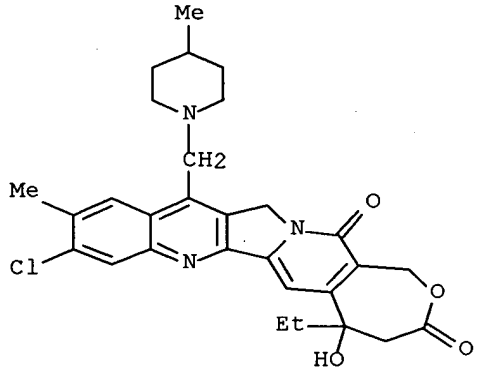
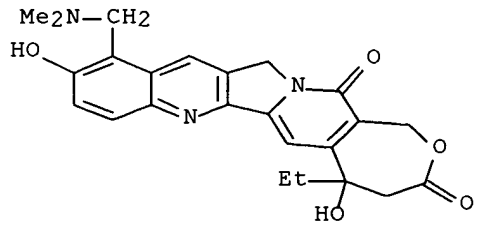


RN 210563-60-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl-12-[(4-methyl-1-piperidinyl)methyl]- (9CI) (CA INDEX NAME)



IT **186668-66-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of camptothecin analogs as antitumors, antivirals, and parasiticides)
RN 186668-66-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



L4 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1998:479535 CAPLUS
DN 129:109247
TI Preparation and formulation of camptothecin analogs as prodrugs for use as
antitumor, antiviral, and parasiticidal agents
IN Bigg, Dennis; Lavergne, Olivier; Harnett, Jerry; Rolland, Alain; Liberatore, Anne-Marie; Lanco, Christophe; et al.
PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S, Fr.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	WO 1997-FR2217	W	19971205		
	WO 1997-FR2218	W	19971205		
	WO 1998-FR1768	W	19980807		
	FR 1999-2398	A	19990226		
	US 1999-332520	A3	19990614		

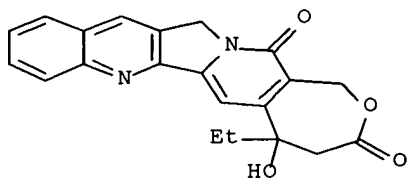
WO 2000-FR461 W 20000224
US 2000-612382 A3 20000707
US 2001-806952 W 20010405
OS MARPAT 129:109247
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

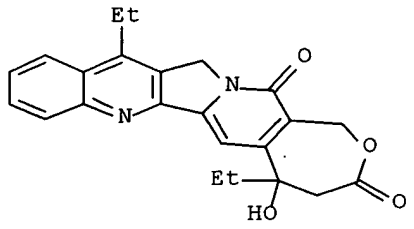
AB Camptothecin analogs I [R1 = alkyl, alkenyl, alkynyl, haloalkyl, etc.; R2 = R3 = R4 = R5 = H, CN, NO2, NHNH2, N3, halo, cyanoalkyl, nitroalkyl, etc.; R16 = H, acyloxy; R17 = alkoxy, amino, etc.; R18 = R19 = H, OH, halo, alkyl, alkoxy; R20 = H, halo; R21 = H, acyl, etc.; R16R17 = bond] were prepd. and formulated as prodrugs for use as antitumor, antiviral, and parasiticidal agents. Thus, camptothecin analog II.HCl was prepd. starting from 2-chloro-4-propionylpyridine, N-(tert-butyloxycarbonyl)glycine, and 3,4-difloroacetanilide via formation of intermediate alc. III and lactone IV, subsequent condensation of the alc. III with the amide moiety of IV, and intramol. cyclocondensation of the resulting chloride. The prepd. compds. were tested for topoisomerase inhibitory activity.

IT **186668-40-6P 186668-44-0P 186668-59-7P**
186668-65-5P 186668-68-8P 186668-69-9P
186668-70-2P 186668-71-3P 186668-72-4P
186668-73-5P 186668-74-6P 186668-75-7P
186668-77-9P 186668-79-1P 186668-90-6P
186668-94-0P 209909-06-8P 209909-08-0P
209909-09-1P 209909-10-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. and formulation of camptothecin analogs as prodrugs for use as antitumor, antiviral, and parasiticidal agents)

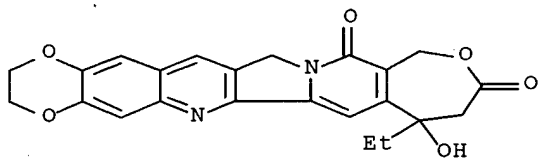
RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



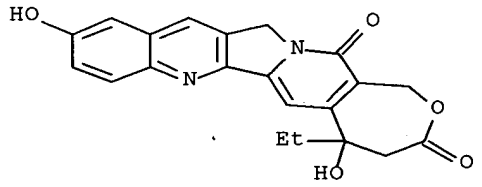
RN 186668-44-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



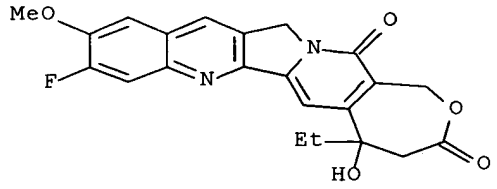
RN 186668-59-7 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-65-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)

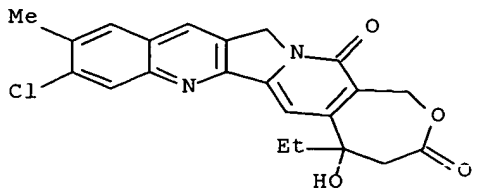


RN 186668-68-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)

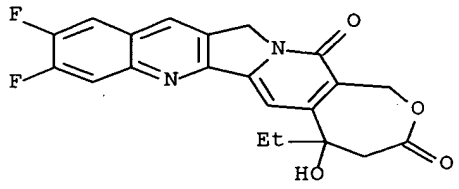


RN 186668-69-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

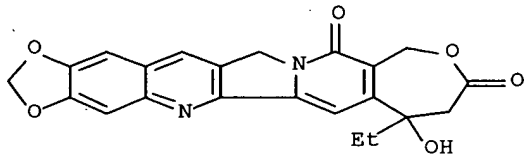
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX
NAME)



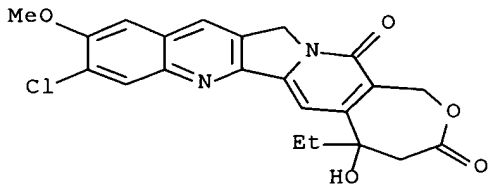
RN 186668-70-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX
NAME)



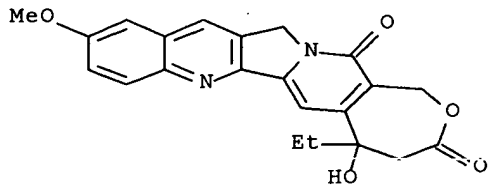
RN 186668-71-3 CAPLUS
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-
dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)



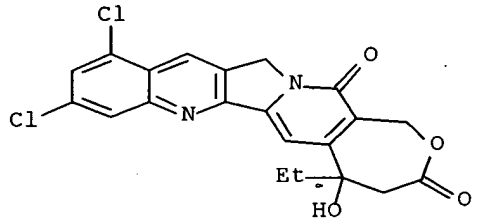
RN 186668-72-4 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA
INDEX NAME)



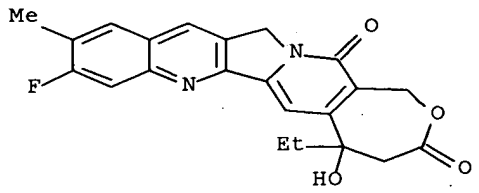
RN 186668-73-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



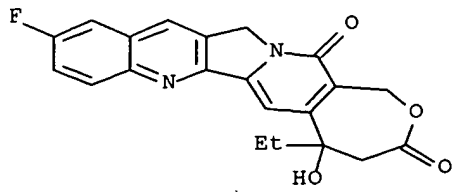
RN 186668-74-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9,11-dichloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



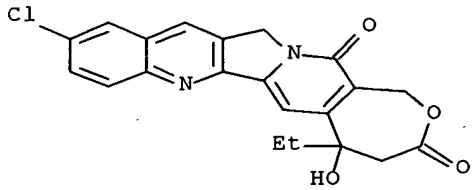
RN 186668-75-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



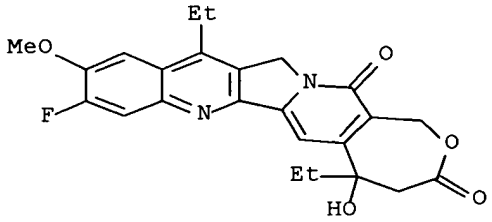
RN 186668-77-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



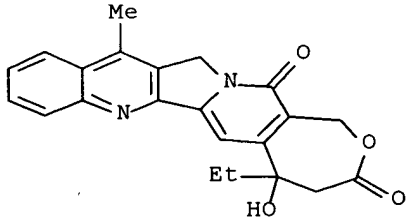
RN 186668-79-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
10-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-90-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5,12-diethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI)
(CA
INDEX NAME)

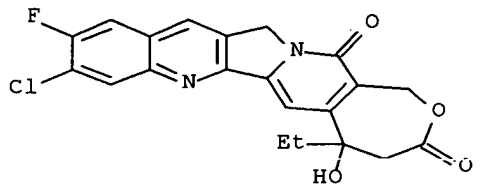


RN 186668-94-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-methyl- (9CI) (CA INDEX NAME)

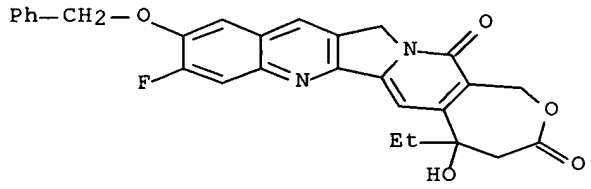


RN 209909-06-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,

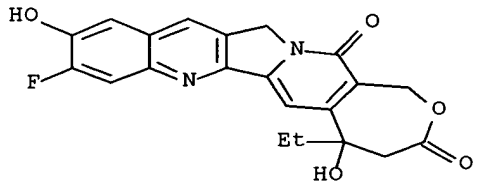
9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX
NAME)



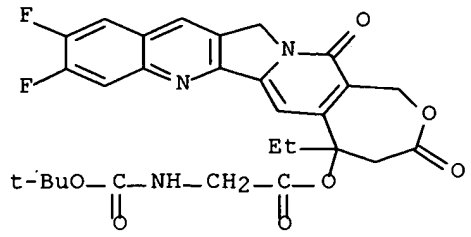
RN 209909-08-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)



RN 209909-09-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)

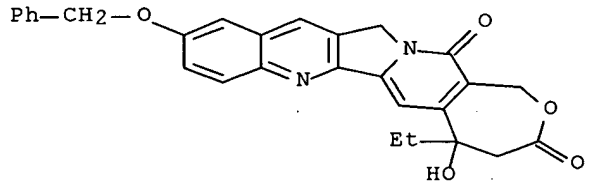


RN 209909-10-4 CAPLUS
CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, 5-ethyl-9,10-difluoro-4,5,13,15-tetrahydro-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-5-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

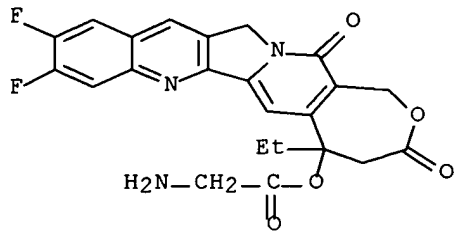


● HCl

IT **186668-63-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(prepn. and formulation of camptothecin analogs as prodrugs for use as
antitumor, antiviral, and parasiticidal agents)
RN 186668-63-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX
NAME)

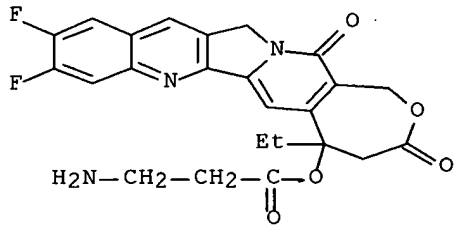


IT **209908-97-4P 209908-98-5P 209908-99-6P**
209909-00-2P 209909-01-3P 209909-02-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and formulation of camptothecin analogs as prodrugs for use as
antitumor, antiviral, and parasiticidal agents)
RN 209908-97-4 CAPLUS
CN Glycine, 5-ethyl-9,10-difluoro-4,5,13,15-tetrahydro-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-5-yl ester, monohydrochloride
(9CI) (CA INDEX NAME)

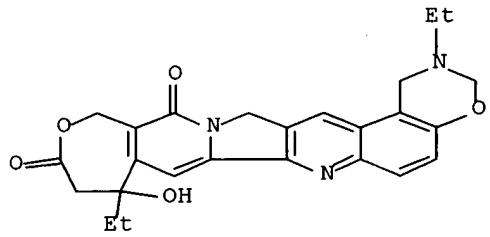


● HCl

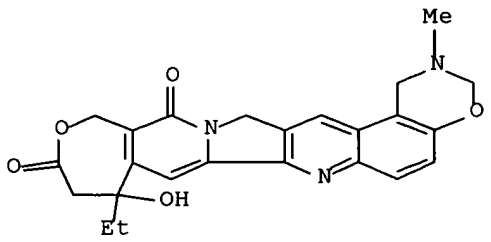
RN 209908-98-5 CAPLUS
CN .beta.-Alanine, 5-ethyl-9,10-difluoro-4,5,13,15-tetrahydro-3,15-dioxo-1H,3H-oxepino[3',4':6,7]indolizino[1,2-b]quinolin-5-yl ester (9CI) (CA INDEX NAME)



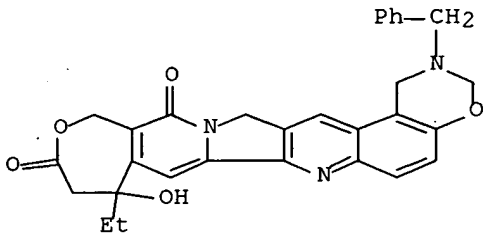
RN 209908-99-6 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 2,9-diethyl-1,2,3,9,10,16-hexahydro-9-hydroxy- (9CI) (CA INDEX NAME)



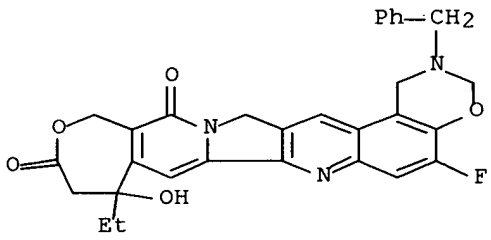
RN 209909-00-2 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 9-ethyl-1,2,3,9,10,16-hexahydro-9-hydroxy-
2-methyl- (9CI) (CA INDEX NAME)



RN 209909-01-3 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 9-ethyl-1,2,3,9,10,16-hexahydro-9-hydroxy-2-(phenylmethyl)- (9CI) (CA INDEX NAME)

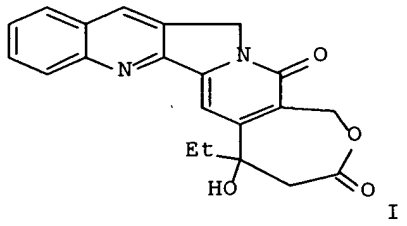


RN 209909-02-4 CAPLUS
CN 13H-Oxepino[3'',4'':6',7']indolizino[2',1':5,6]pyrido[3,2-f][1,3]benzoxazine-11,14-dione, 9-ethyl-5-fluoro-1,2,3,9,10,16-hexahydro-9-hydroxy-2-(phenylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1997:633920 CAPLUS
DN 127:331621
TI BN 80245: an E-ring modified camptothecin with potent antiproliferative and topoisomerase I inhibitory activities
AU Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Bigg, Dennis C. H.
CS Inst. Henri Beaufour, Les Ulis, F-91966, Fr.
SO Bioorganic & Medicinal Chemistry Letters (1997), 7(17), 2235-2238
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier
DT Journal
LA English
GI

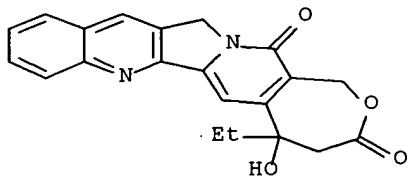


I

AB The crucial E-ring of camptothecin was modified to afford the homologous .beta.-hydroxylactone deriv. BN 80245 (I). This compd., which is more stable than camptothecin, remains a potent inhibitor of both cell growth and topoisomerase I.

IT **186668-40-6P**, BN 80245
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of BN 80245, an E-ring modified camptothecin, with potent antiproliferative and topoisomerase I inhibitory activities)

RN 186668-40-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2003 ACS
AN 1997:140288 CAPLUS
DN 126:144433
TI Preparation of novel camptothecin analogs as antitumor agents
IN Bigg, Dennis; Lavergne, Olivier; Pla, Rodas Francesc; Pommier, Jacques; Ulibarri, Gerard
PA Societe De Conseils De Recherches Et D'application, Fr.; Bigg, Dennis; Lavergne, Olivier; Pla Rodas, Francesc; Pommier, Jacques; Ulibarri, Gerard
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9700876	A1	19970109	WO 1996-FR980	19960621
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
	CA 2225528	AA	19970109	CA 1996-2225528	19960621
	AU 9664608	A1	19970122	AU 1996-64608	19960621
	AU 716377	B2	20000224		
	ZA 9605318	A	19970124	ZA 1996-5318	19960621
	EP 835258	A1	19980415	EP 1996-924010	19960621
	EP 835258	B1	20020925		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, LT, LV, FI				
	CN 1192740	A	19980909	CN 1996-196127	19960621
	BR 9608639	A	19990629	BR 1996-8639	19960621
	JP 11508249	T2	19990721	JP 1996-503644	19960621
	NZ 312715	A	20000128	NZ 1996-312715	19960621
	RU 2164515	C2	20010327	RU 1998-101135	19960621
	IL 128044	A1	20010430	IL 1996-128044	19960621
	IL 122635	A1	20011031	IL 1996-122635	19960621
	RO 117918	B1	20020930	RO 1997-2400	19960621
	AT 224900	E	20021015	AT 1996-924010	19960621
	EP 1251125	A2	20021023	EP 2002-77736	19960621
	EP 1251125	A3	20021211		
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	TW 457234	B	20011001	TW 1996-85109645	19960808
	US 5981542	A	19991109	US 1997-973561	19971202
	NO 9705988	A	19980219	NO 1997-5988	19971219
	US 6313135	B1	20011106	US 1999-325913	19990604
	US 6339091	B1	20020115	US 1999-332520	19990614
	US 2002160994	A1	20021031	US 2002-61049	20020130
	US 2003004150	A1	20030102	US 2002-71046	20020206
PRAI	GB 1995-12670	A	19950621		
	US 1996-610476	A	19960304		
	EP 1996-924010	A3	19960621		
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	FR 1996-15775	A	19961220
	FR 1996-15945	A	19961224
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	US 2001-806952	W	20010405

OS MARPAT 126:144433

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A camptothecin analogs I and II (R1 = alkyl, alkenyl, alkynyl, alkoxy, alkylthio; R2, R3, R4 R5 = independently, H, halo, alkyl, cyano, azido, hydrazino, heterocyclic substituted alkyl or acyl; R16 = H, alkoxy; R17 = alkoxy, amino, heterocyclic amino; R18, R19 = independently, H, halo, OH, alkyl, alkoxy; R20 = H, halo) were prepd. by a variety of synthetic paths and were tested for topoisomerase I inhibiting activity as antitumor agents. Thus, camptothecin analog III was prepd. form 7-ethylcamptothecin and reduced topoisomerase I activity to 96.9% at 10 .mu.M and 20.4% at 500 .mu.M of control activity levels. Camptothecin analog III was also tested against various tumor cell lines such as L1210 and HCT15.

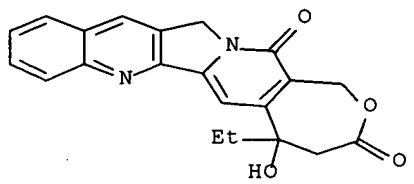
IT **186668-40-6P 186668-44-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

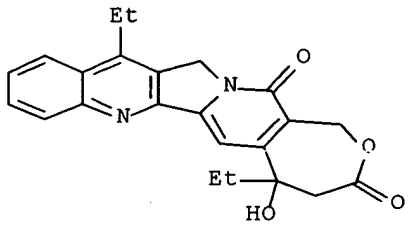
(prepn. of camptothecin analogs as antitumor agents)

RN 186668-40-6 CAPLUS

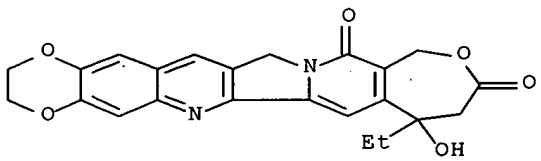
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



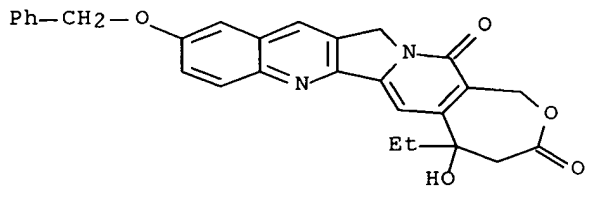
RN 186668-44-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5,12-diethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



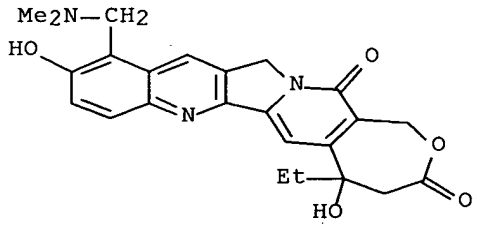
IT **186668-59-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-59-7 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy- (9CI) (CA INDEX NAME)



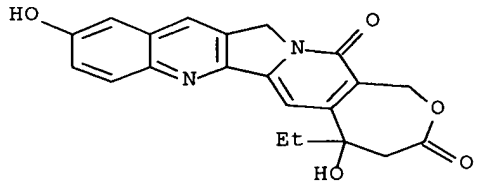
IT **186668-63-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-63-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-(phenylmethoxy)- (9CI) (CA INDEX NAME)



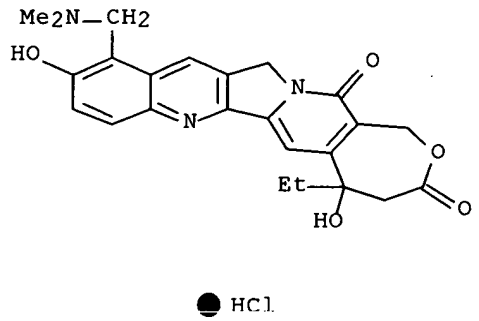
IT **186668-66-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-66-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)



IT **186668-65-5P 186668-67-7P 186668-68-8P**
186668-69-9P 186668-70-2P 186668-71-3P
186668-72-4P 186668-73-5P 186668-74-6P
186668-75-7P 186668-77-9P 186668-79-1P
186668-81-5P 186668-83-7P 186668-90-6P
186668-94-0P 186669-03-4P 186669-04-5P
186669-06-7P 186669-07-8P 186669-08-9P
186669-09-0P 186669-10-3P 186669-12-5P
186669-13-6P 186669-14-7P 186669-16-9P
186669-18-1P 186669-19-2P 186669-20-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of camptothecin analogs as antitumor agents)
RN 186668-65-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy- (9CI) (CA INDEX NAME)

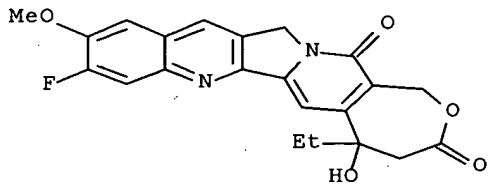


RN 186668-67-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 11-[(dimethylamino)methyl]-5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-, monohydrochloride (9CI) (CA INDEX NAME)

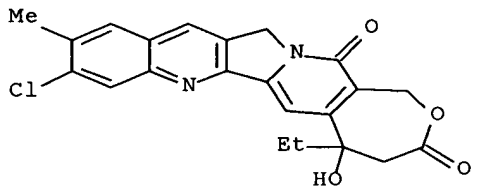


● HCl

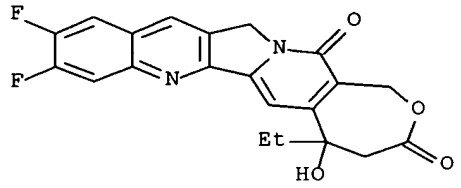
RN 186668-68-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



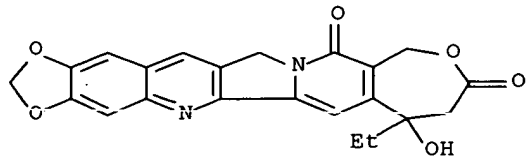
RN 186668-69-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methyl- (9CI) (CA INDEX NAME)



RN 186668-70-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9,10-difluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



RN 186668-71-3 CAPLUS
CN 9H,12H-1,3-Dioxolo[4,5-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-9,12-
dione, 7-ethyl-7,8,11,14-tetrahydro-7-hydroxy- (9CI) (CA INDEX NAME)



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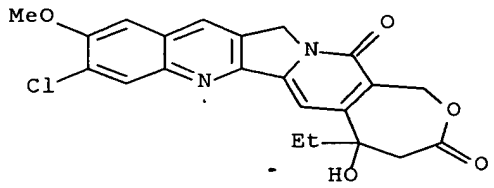
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



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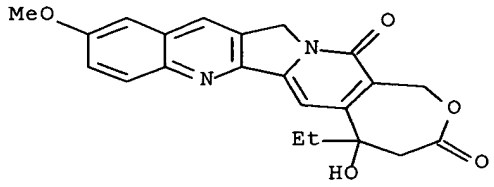
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy- (9CI) (CA INDEX NAME)



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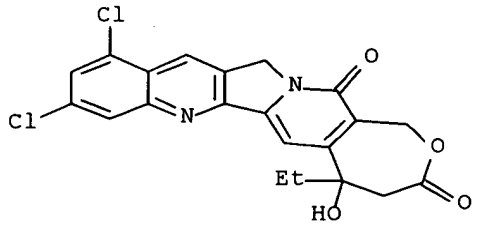
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
9,11-dichloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



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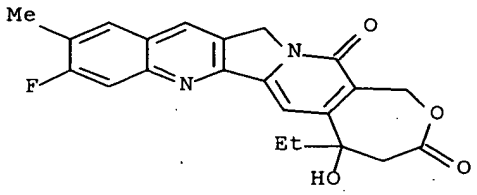

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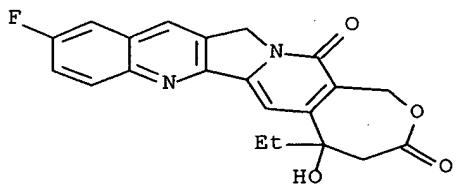
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



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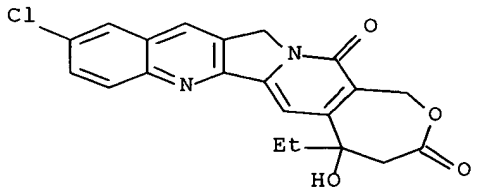
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 10-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy- (9CI) (CA INDEX NAME)



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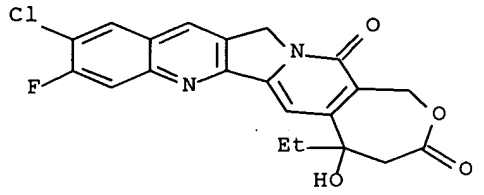
NAME)



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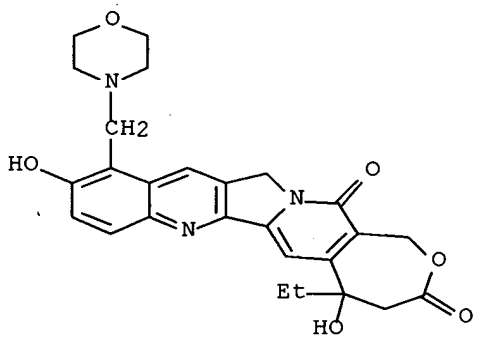
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5,10-dihydroxy-11-(4-morpholinylmethyl)-
(9CI)
(CA INDEX NAME)



RN 186668-90-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
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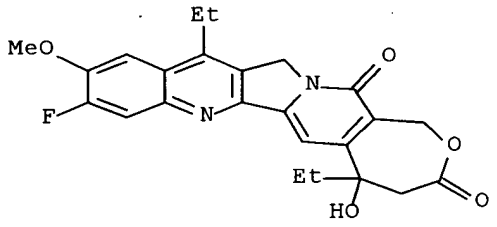
(CA
INDEX NAME)



RN 186668-94-0 CAPLUS
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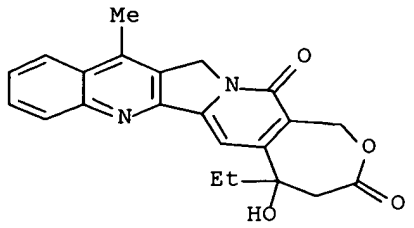
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-methyl- (9CI) (CA INDEX NAME)



RN 186669-03-4 CAPLUS
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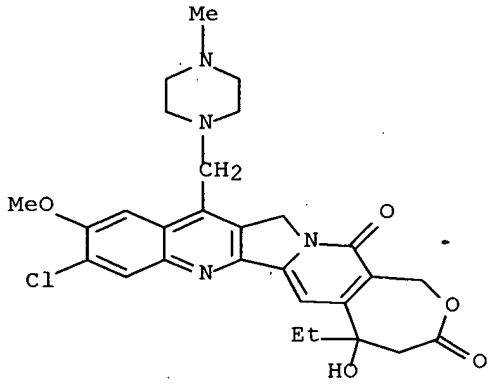
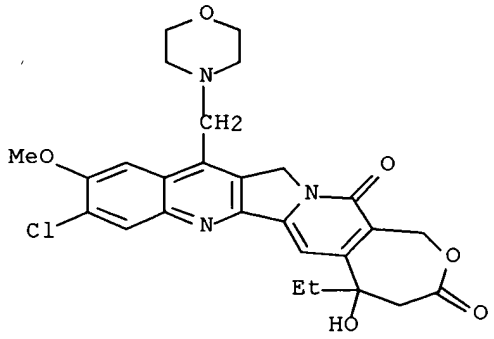
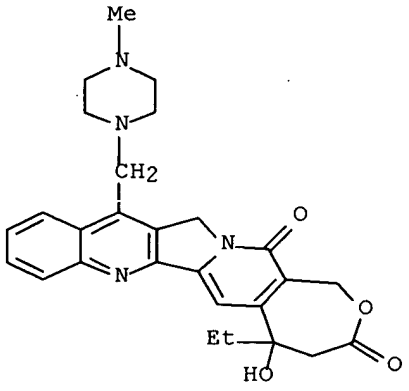


RN 186669-04-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-10-methoxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)

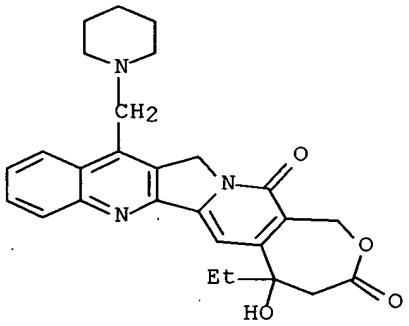


RN 186669-06-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]-

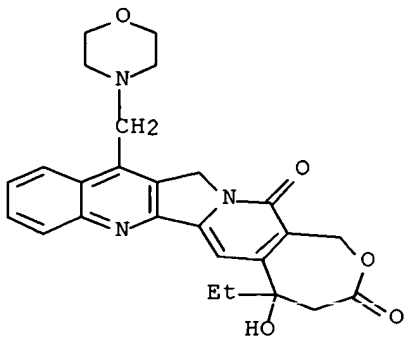
(9CI) (CA INDEX NAME)



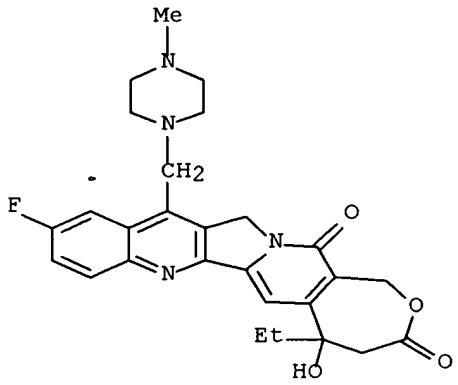
RN 186669-07-8 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI)
(CA
INDEX NAME)



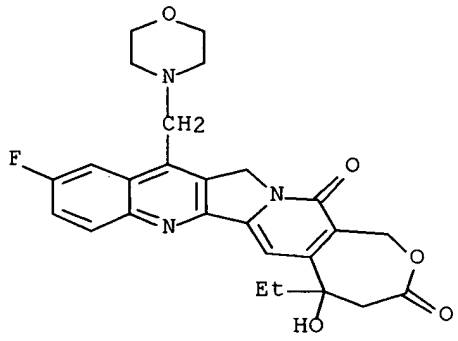
RN 186669-08-9 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione,
5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI)
(CA
INDEX NAME)



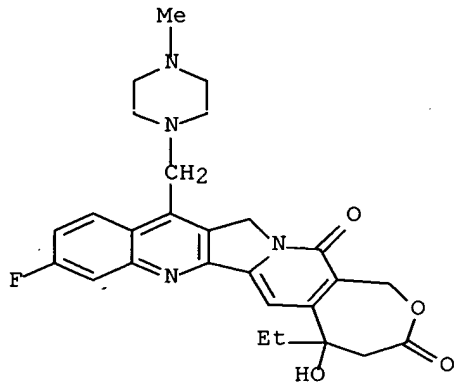
RN 186669-09-0 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



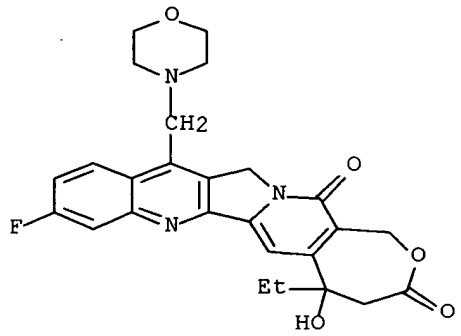
RN 186669-10-3 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)-
(9CI) (CA INDEX NAME)



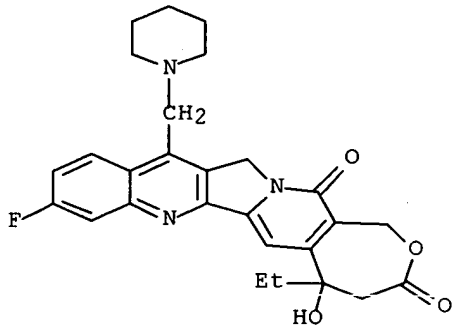
RN 186669-12-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)



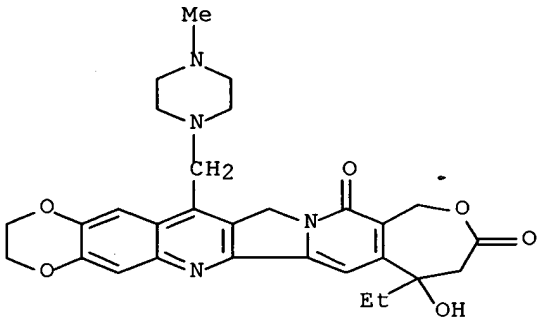
RN 186669-13-6 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



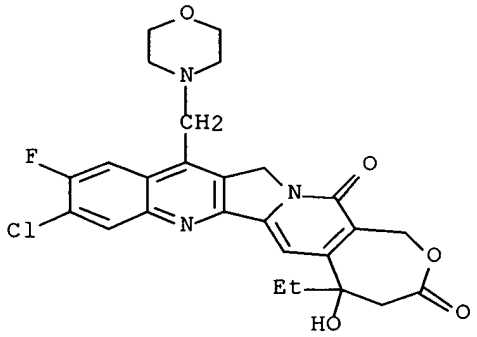
RN 186669-14-7 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-9-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(1-piperidinylmethyl)- (9CI) (CA INDEX NAME)



RN 186669-16-9 CAPLUS
CN 10H,13H-1,4-Dioxino[2,3-g]oxepino[3',4':6,7]indolizino[1,2-b]quinoline-10,13-dione, 8-ethyl-2,3,8,9,12,15-hexahydro-8-hydroxy-16-[(4-methyl-1-piperazinyl)methyl]- (9CI) (CA INDEX NAME)

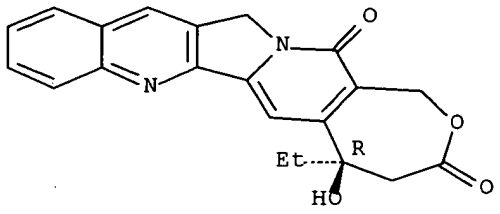


RN 186669-18-1 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 9-chloro-5-ethyl-10-fluoro-1,4,5,13-tetrahydro-5-hydroxy-12-(4-morpholinylmethyl)- (9CI) (CA INDEX NAME)



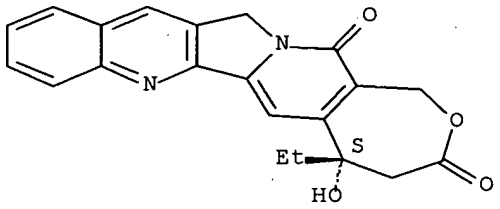
RN 186669-19-2 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

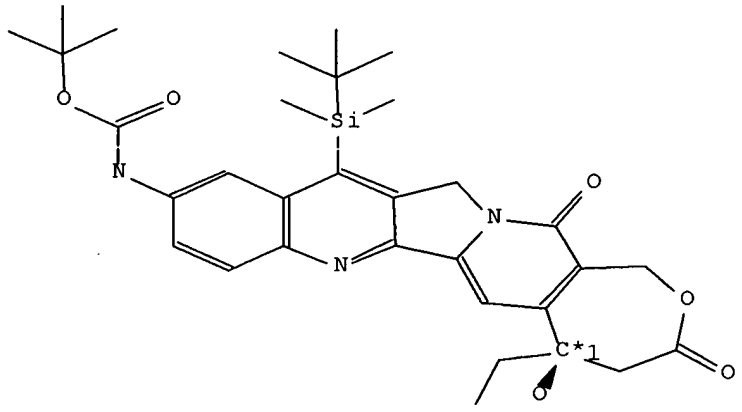


RN 186669-20-5 CAPLUS
CN 3H,15H-Oxepino[3',4':6,7]indolizino[1,2-b]quinoline-3,15-dione, 5-ethyl-1,4,5,13-tetrahydro-5-hydroxy-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



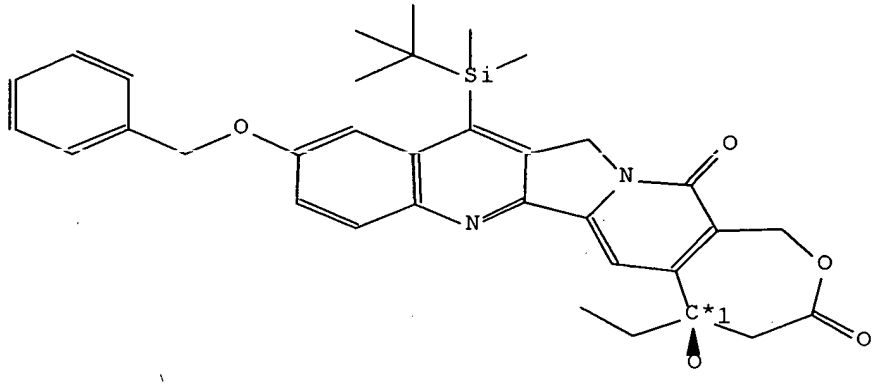
L8 ANSWER 1 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



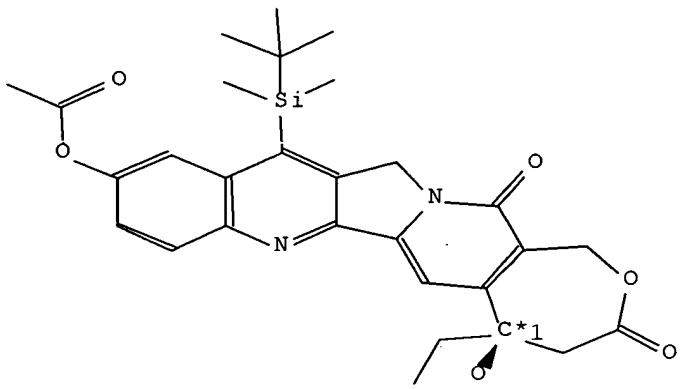
Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

Crystal Property Description:
CPD
(CPD): light-brown
Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

L8 ANSWER 2 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



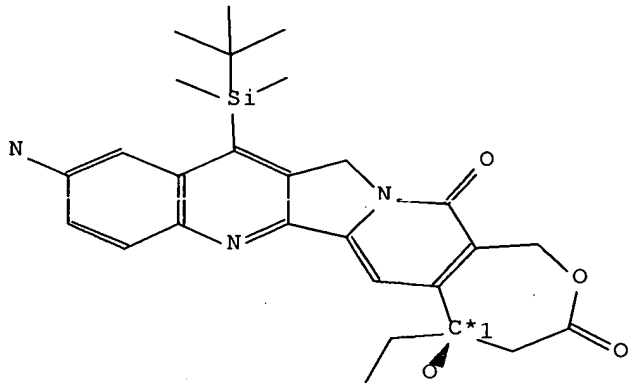
L8 ANSWER 3 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

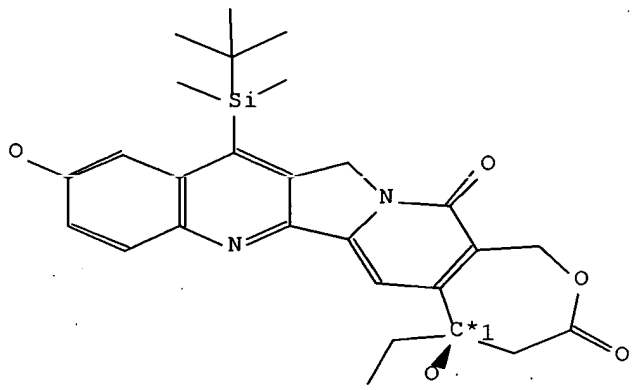
L8 ANSWER 4 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

Crystal Property Description:
CPD
(CPD): yellow
Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

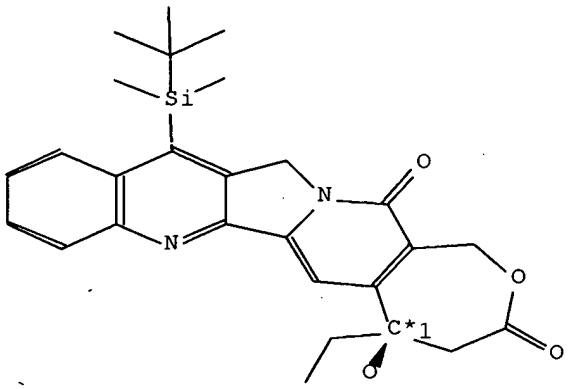
L8 ANSWER 5 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

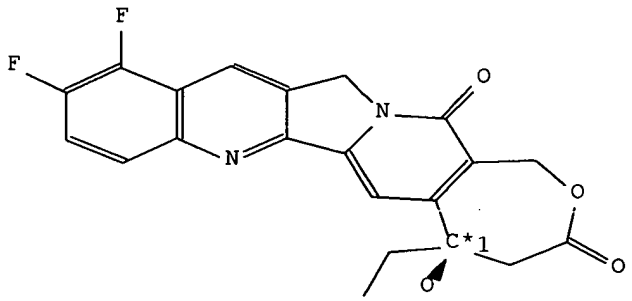
L8 ANSWER 6 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

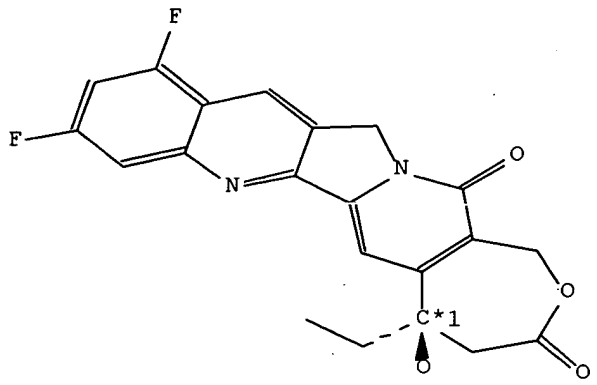
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

L8 ANSWER 7 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

L8 ANSWER 8 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL

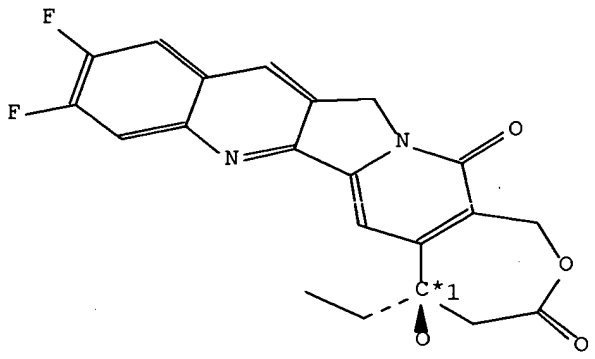


Atom/Bond Notes:
1. CIP Descriptor: R

Field Availability:

Reference(s):
1. Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Breton, Christine Le; et al., J.Med.Chem., CODEN: JMCMAR, 43(11), <2000>, 2285 - 2289; BABS-6280660

L8 ANSWER 9 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL

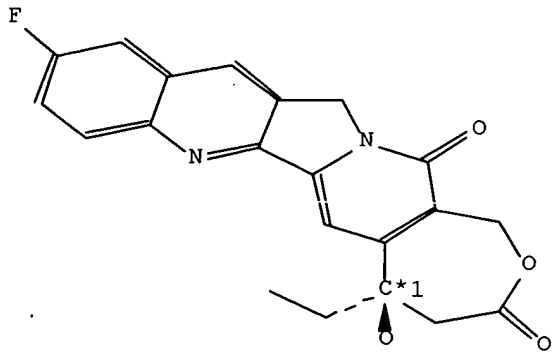


Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

NMR

Coupling Nuclei (.NUI) 19F-13C
Solvents (.SOL): dimethylsulfoxide-d6
Reference(s):
1. Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Breton, Christine Le; et al., J.Med.Chem., CODEN: JMCMAR, 43(11), <2000>, 2285 - 2289; BABS-6280660

L8 ANSWER 10 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



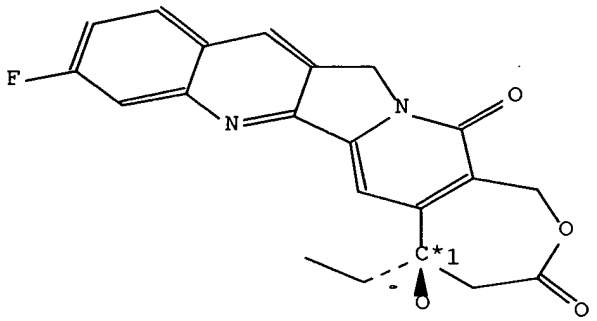
Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

NMR

Coupling Nuclei (.NUI) 19F-13C
Solvents (.SOL): dimethylsulfoxide-d6
Reference(s):
1. Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Breton, Christine Le; et al., J.Med.Chem., CODEN: JMCMAR, 43(11), <2000>, 2285 - 2289; BABS-6280660

L8 ANSWER 11 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL

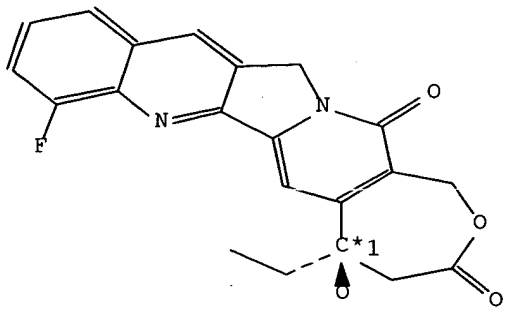
Beilstein Records (BRN):	8805073
Chemical Name (CN):	(R)-11-fluorohomocamptothecin
Molec. Formula (MF):	C21 H17 F N2 O4
Molecular Weight (MW):	380.37
Lawson Number (LN):	32176
File Segment (FS):	Stereo compound
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	7453021
Tautomer ID (TAUTID):	8290716
Entry Date (DED):	2001/07/25
Update Date (DUPD):	2003/01/18



Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

Reference(s):
1. Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Breton, Christine Le; et al., J.Med.Chem., CODEN: JMCMAR, 43(11), <2000>, 2285 - 2289; BABS-6280660

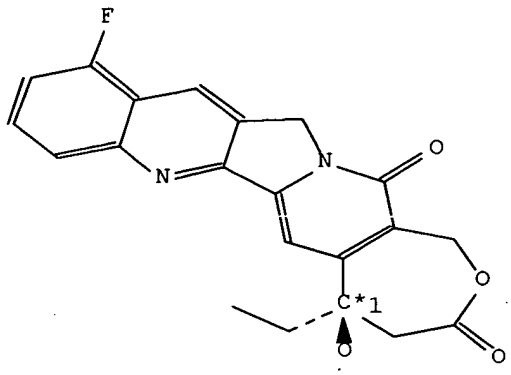
L8 ANSWER 12 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

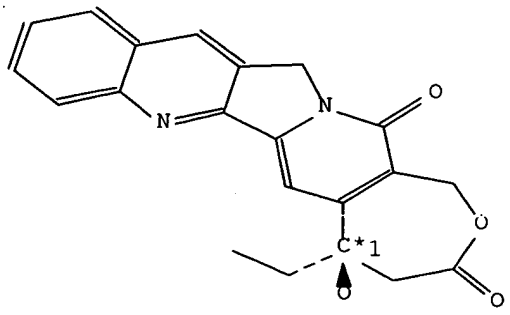
L8 ANSWER 13 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):
1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

Reference(s):
1. Lavergne, Olivier; Demarquay, Daniele; Bailly, Christian; Lanco, Christophe; Rolland, Alain; Huchet, Marion; Coulomb, Helene; Muller, Nicole; Baroggi, Nicole; Camara, Jose; Breton, Christine Le; et al., J.Med.Chem., CODEN: JMCMAR, 43(11), <2000>, 2285 - 2289; BABS-6280660

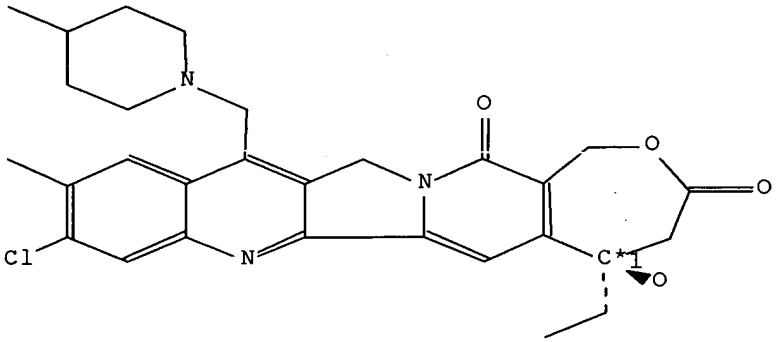
L8 ANSWER 14 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



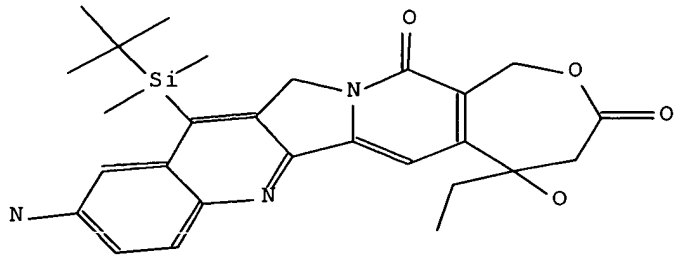
Reference(s):

1. Gabarda, Ana E.; Du, Wu; Isarno, Thomas; Tangirala, Raghuram S.; Curran, Dennis P., Tetrahedron, CODEN: TETRAB, 58(32), <2002>, 6329 - 6342; BABS-6360059

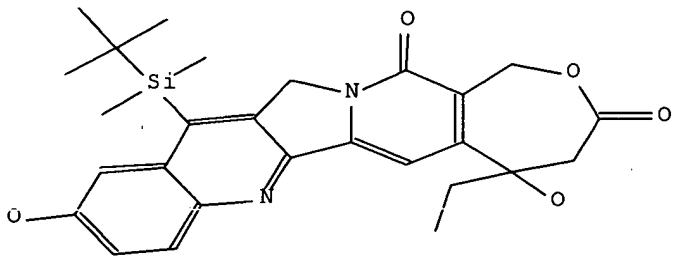
L8 ANSWER 15 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



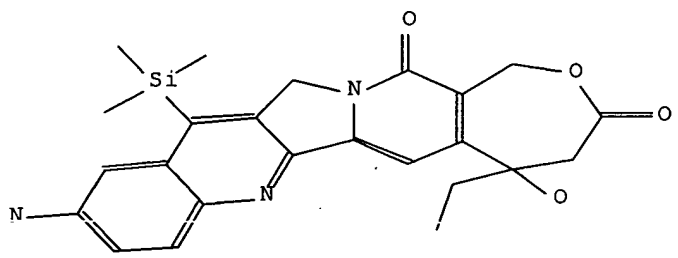
L8 ANSWER 16 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



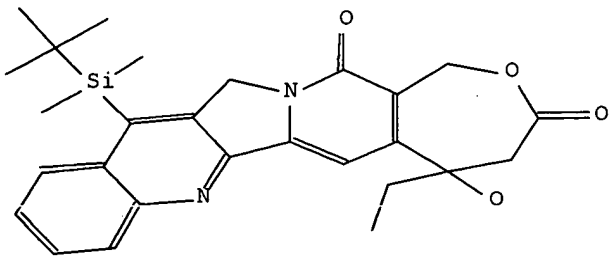
L8 ANSWER 17 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



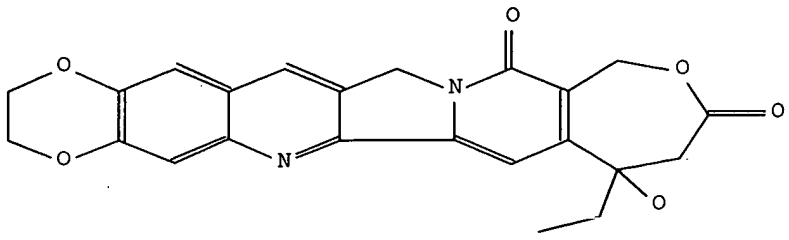
L8 ANSWER 18 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



L8 ANSWER 19 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



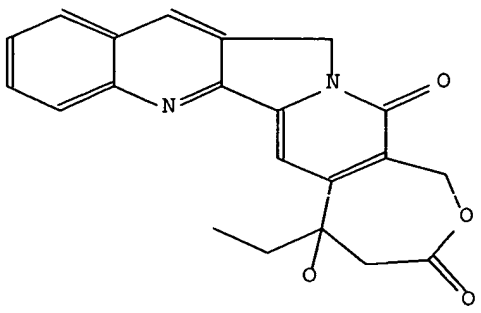
L8 ANSWER 20 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

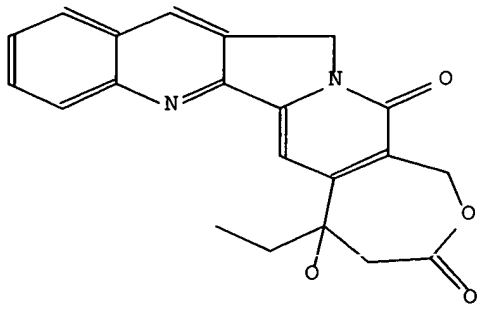
L8 ANSWER 21 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

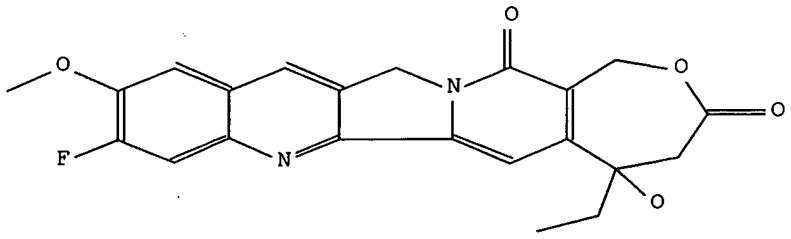
L8 ANSWER 22 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

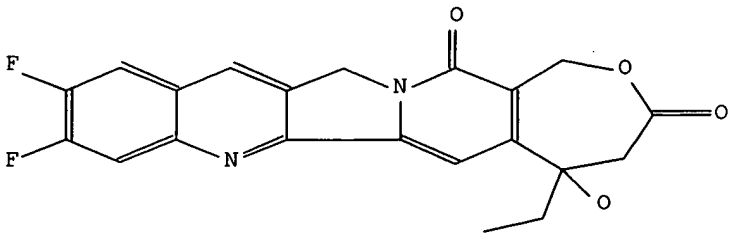
L8 ANSWER 23 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):
1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

Reference(s):
1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

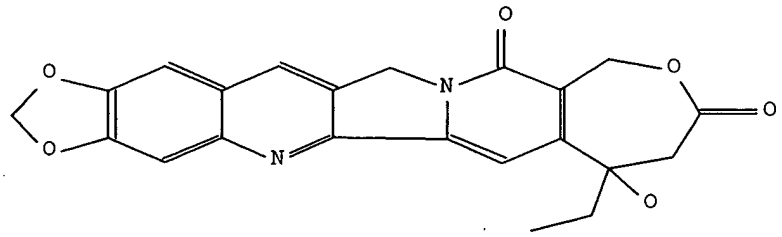
L8 ANSWER 24 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

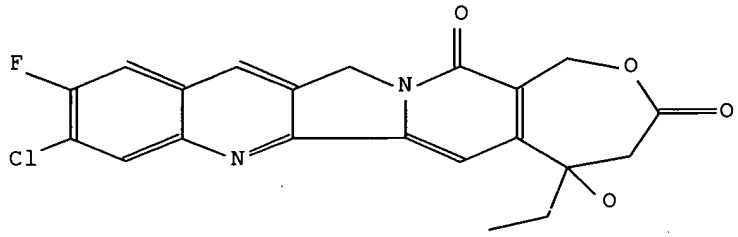
L8 ANSWER 25 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

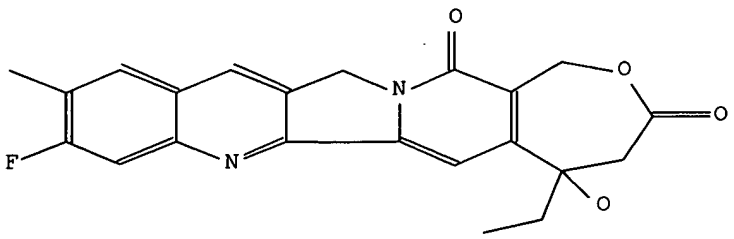
L8 ANSWER 26 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

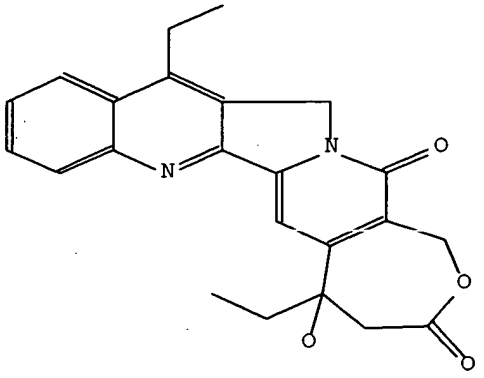
L8 ANSWER 27 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

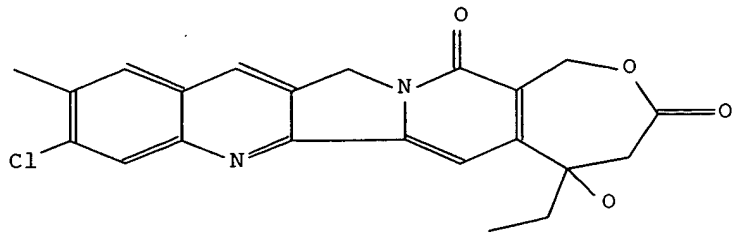
L8 ANSWER 28 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

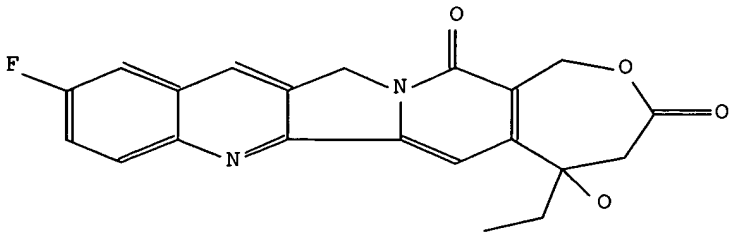
L8 ANSWER 29 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

L8 ANSWER 30 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



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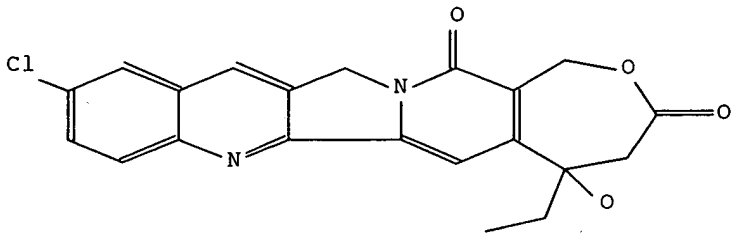
1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

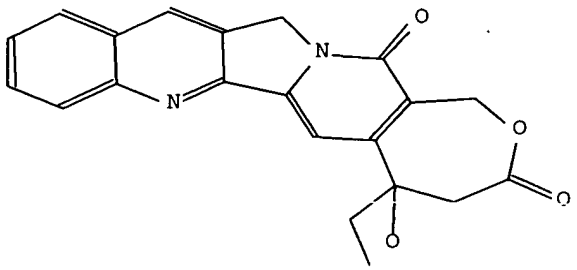
L8 ANSWER 31 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

L8 ANSWER 32 OF 32 BEILSTEIN COPYRIGHT 2003 BEILSTEIN CDS MDL



Reference(s):

1. Lavergne, Olivier; Lesueur-Ginot, Laurence; Rodas, Francesc Pla; Kasprzyk, Philip G.; Pommier, Jacques; et al., J.Med.Chem., CODEN: JMCMAR, 41(27), <1998>, 5410 - 5419; BABS-6162156

L11 ANSWER 1 OF 1 MARPAT COPYRIGHT 2003 ACS
AN 136:310067 MARPAT
TI Preparation of silyl camptothecins and silyl homocamptothecins
IN Curran, Dennis P.; Du, Wu
PA University of Pittsburgh, USA
SO U.S., 17 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6372906	B1	20020416	US 2001-833757	20010412
WO 2002083694	A1	20021024	WO 2002-US11139	20020409

PI

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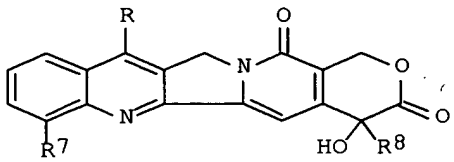
PRAI US 2001-833757 20010412
OS CASREACT 136:310067
GI



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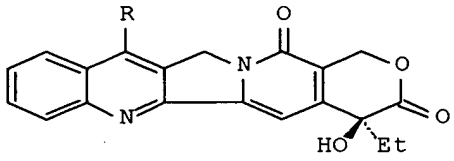
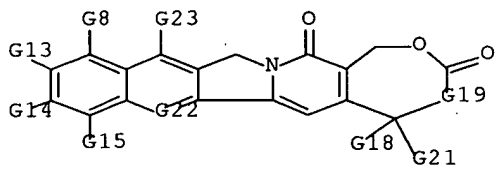


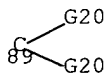
II

AB Prepn. of silylated camptothecins, such as I [R, R7 = SiR1R2R3; R1, R2, R3 = H, alkyl, cycloalkyl, alkenyl, alkynyl, aryl, etc.; R8 = benzyl, alkyl, hydroxyalkyl, alkenyl, alkynyl,], which are useful intermediates in the synthesis of camptothecin antitumor agents, was described. Thus, 7-silylated camptothecin deriv. II (R = SiMe2CMe3) was prepd. in 60% yield by refluxing camptothecin II (R = H), Me3CSiMe2H, (Me2CH)3SiSH, and di-tert-Bu peroxide in p-dioxane under argon for 36 h.

MSTR 1



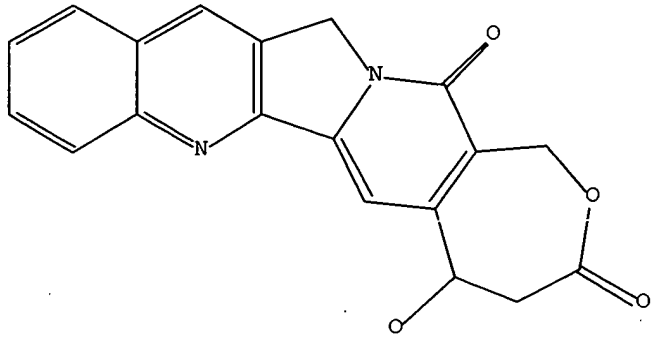
G19 = 89



G21 = OH
G22 = N
MPL: claim 1
STE: or enantiomers

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l1; d his; log y
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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L1 STRUCTURE UPLOADED
L2 5 S L1
L3 215 S L1 FUL

FILE 'CAPLUS' ENTERED AT 11:54:49 ON 30 APR 2003
L4 32 S L3

FILE 'BEILSTEIN' ENTERED AT 11:56:34 ON 30 APR 2003
L5 3 S L1
L6 32 S L1 FUL
L7 32 S L6 NOT L3
L8 32 S L6 NOT L4

FILE 'MARPAT' ENTERED AT 11:58:20 ON 30 APR 2003
L9 0 S L1
L10 9 S L1 FUL
L11 1 S L10 NOT L4

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